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PATHOLOGY
FOR
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An exhaustive bibliography is included in the third volume, (pages 2225 to 2452), with references to the literature of Germany, France, Spain, Italy, Sweden, Switzerland, Denmark, Portugal, Russia, England and the United States.

For greater convenience a complete index is included in each volume and the volume number is printed in italics. The references to illustrations are in bold face type.

While there is in the text a complete system of cross references to related subjects the index summarizes them for ready reference. Example, under the heading "Abscesses" there are 76 entries.

PATHOLOGY

FOR STUDENTS
AND PRACTITIONER'S

Authorized Translation of the
Lehrbuch der Pathologischen Anatomie

BY
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IN THREE VOLUMES 1072 ILLUSTRATIONS

VOLUME II

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CONTENTS

VOLUME II

CHAPTER PAGE
IV. DIGESTIVE ORGANS. (CONTINUED FROM VOLUME I) 817
V. DISEASES OF THE OSSEOUS SYSTEM 1051
VI. DISEASES OF JOINTS. DIARTHROSES AND SYNARTHROSES . . 1228
VII. ADRENAL GLANDS 1276
VIII. URINARY APPARATUS 1292
IX. SEX ORGANS. (CONTINUED IN VOLUME III) 1458
INDEX FOR COMPLETE WORK . . . . I–LXII

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The author saw a mucoid adenocarcinoma in a 32 year old man. Carcinomas of the appendix are relatively rare, favoring individuals between the 2nd and 4th decades. The youngest case was 8 years old, the oldest, 92 (see Kudo, lit.). Usually they are small, to the size of a pea, rarely as large as a walnut (Elting), or to a child's fist (Kudo); on section they are yellowish-white and cloudy, due to deposits of doubly refracting lipoids (see Maresch, Hada). Perhaps an inflammation prepares the ground for the carcinoma (Harte). Milner declares that the carcinomas of the appendix in the literature are purely inflammatory neoplasms in which the proliferating endothelium of the lymph spaces imitates strands of carcinoma cells; Neugebauer thinks the small tumors in the distal end are endotheliomas, but his views have not been accepted (s. Dietrich, Konjetzny, Winkler and lit. in appendix). There is no question but that they are epithelial neoplasms and some are surely carcinomas. This conception which is likewise applied to the small tumors of the small bowel (see following) is expressed more and more in the newer

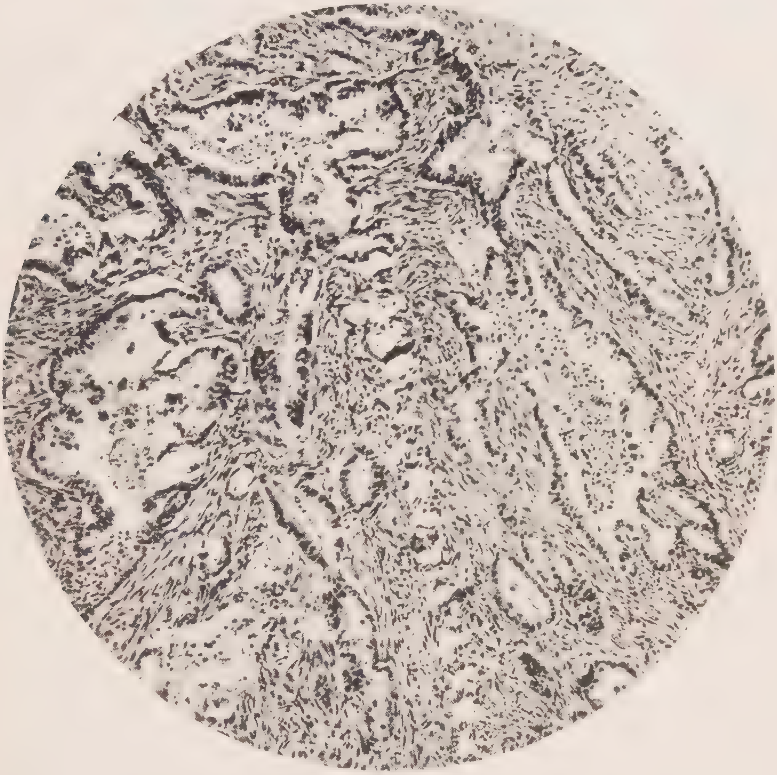


FIG. 386.—Secondary adeno carcinoma of the wall of the vermiform appendix. Primary tumor in the cecum. Compare with Fig. 385. × 100. L. H. #6240.

literature, but metastases and recurrences have been noted (Batzdorf, lit.; lit. in appendix).

Much discussed and closely parallel to the small carcinomas of the appendix, are the small, occasionally multiple, epithelial tumors of the small bowel, which are white yellow on section from lipoids within the cells. They are designated by some as slow growing carcinomas (Zaayer, Oberndorfer, Verse, J. L. Burckhardt, and others), but others consider them benign epithelial tumors, in spite of their morphological identity to carcinoma (carcinoids, Oberndorfer and others); some believe they are heterotopic cell complexes in the submucosa (Toennissen, lit.), or pancreatic rests, or misplaced islands of Langerhans of the pancreas (Saltykow).

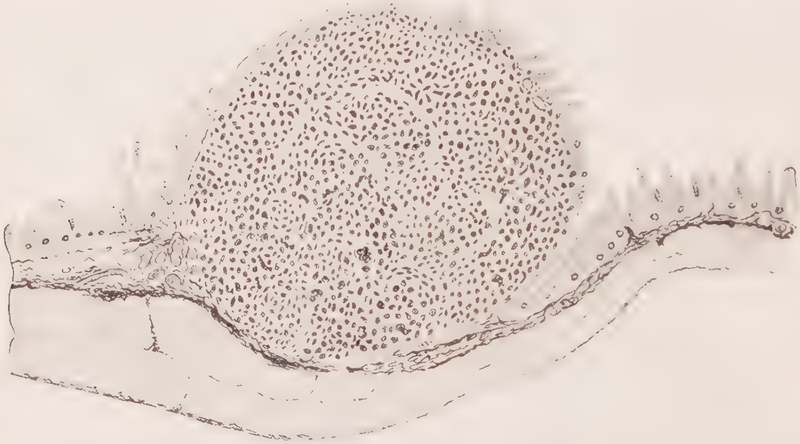


FIG. 387.—a. Small carcinoma of ileum of man 63; located chiefly in submucosa; muscularis mucosae is broken through. Elastin stain. Magnifying glass.

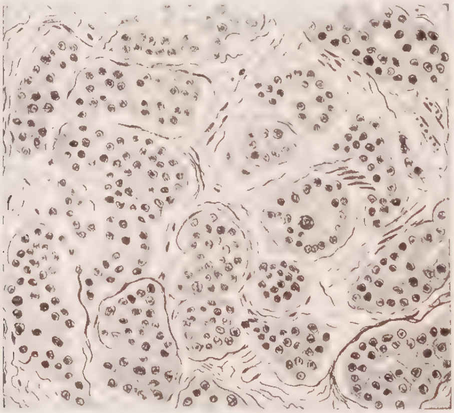


FIG. 388.—b. Small carcinoma of ileum. Carc. solidum with indication of gland imitations. Detail of fig. 387.—a. (Higher power).

Thus they are called tumor-like malformations, "hamartomas," or "choristomas" (hamartoma, from the Greek—failure; choristoma, from the Greek—separate) (Gerlach). But then they should be called choristoblastomas, since they are not merely split-off epithelial cells, but actual blastomas—tumor-like proliferations—which were derived from these supposed germinal rests. The cells, often remarkably uniform, rounded or polygonal, are grouped in nests, within which isolated gland-like lumena or merely holes are differentiated; mitoses are absent, the alveolar scaffolding is devoid of reaction and without small cell infiltration. A relation to the glands is often demonstrable (the author; J. L. Burckhardt). Krompecher speaks of a benign and a malignant solid basalioma or basal cell carcinoma in contradistinction to the glandular, so-called adenoid basal cell carcinoma, as they occur in other cylindrical epithelial mucosae. J. L. Burckhardt had previously used the term basal cell carcinoma. The author supports this idea. Just as there are transitions of benign to malignant basaliomas, of epitheliomas to carcinomas in other places, and just as difficult as it is in other situations (cf. skin) to determine the actual border line, so it is difficult in these small epithelial tumors of the small

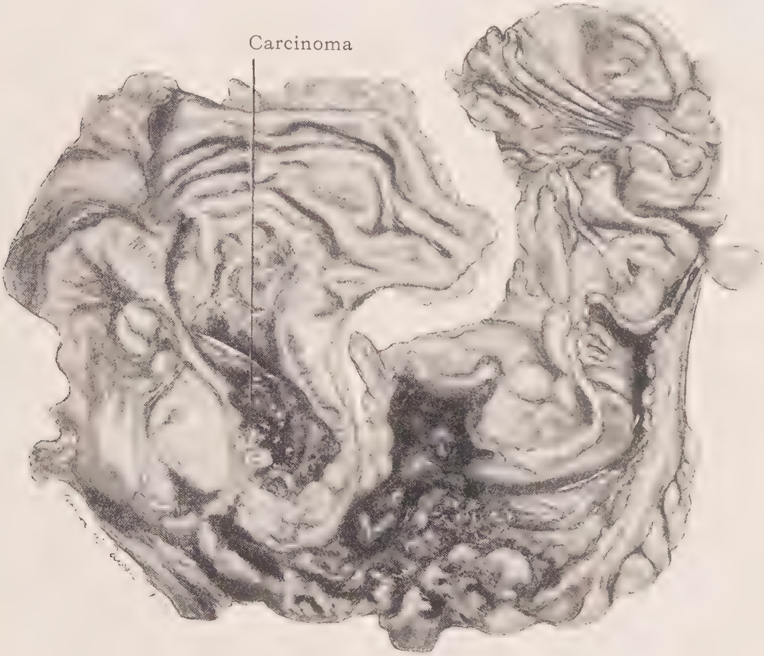


FIG. 389.—Carcinoma of the sigmoid. Operative specimen from a man 60 years old. According to the symptoms, this was present for 15 months, resignation to surgical measures being agreed to by the patient on account of acute intestinal obstruction. The mass was polypoid and ulcerated and had extended through the walls to appear on the outer surface. A few metastatic nodes were found in the immediate mesentery. L. H. #19579.

bowel. The morphological character corresponds to that of carcinoma. Generally speaking, these small intestinal carcinomas share a relative benign character with the basal cell carcinomas. But pronounced cylindrical cell solid carcinomas, which sometimes show beginning cylindroma formation, deep infiltration of the wall, stenosis, etc., develop into clinical carcinomas (fig. 307). There are still other cases in which metastases occur, but the primary tumor cannot be differentiated by structure from a "benign carcinoma" of the small intestine (Verse, B. M. Schmidt, Dietrich, Schopper, Tuxen). Gerlach suggests separating these special carcinomas of basalioma structure from the common carcinomas of the small bowel of adenocarcinomatous or round cell carcinomatous character, but this proposition must be restricted because transitions are possible from the solid to the so-called adenoid basal cell carcinoma, or from the latter to the complex, even gyriform adenocarcinoma (fig. 372). (The term "carcinoid" should not be used, since it is merely an expression of perplexity.)

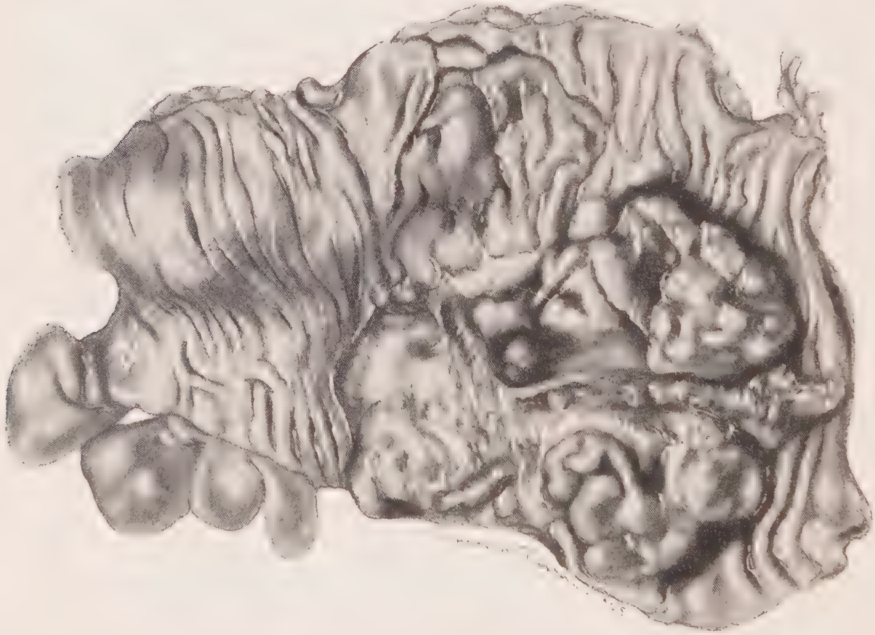


Fig. 390.—Carcinoma of the sigmoid. This tumor was definitely polypoid and had not as yet extended annularly sufficient to produce total obstruction. Attention was called to the patient by the presence of bloody mucus and purulent material in the stools. The surfaces of the growth were ulcerated and bathed in a necrotic purulent fluid. No metastases were detected at operation. L. H. #19701.

Consequences of carcinoma are: stenosis which may appear quite sudden, up to total occlusion of the bowel, either by the tumor itself or by a form of invagination (Kraske). Perforation from disintegration of the tumor is frequent into the peritoneum or into hollow organs, with the formation of fistulae or broader communications; thus, between the colon and stomach, rectum and ileum, bladder, etc., adhesions from secondary inflammation frequently kink and obstruct the bowel, usually in carcinomas in the lower parts. Hemorrhages from the disintegrating tumor tissue are usually not dangerous. The base of the ulcer may suppurate. Hypertrophy and dilatation occur above the stenosis, as in fig. 391; the transverse colon opened above a small stenosing carcinoma of the splenic flexure, which resembles that in fig. 384; it is 32 cm. broad. Distension ulcers may appear in the dilated portions, *i.e.*, decubital ulcers, as well as stercoreal diphtheria which often leads to chronic peritonitis with adhesions, or to acute peritonitis from escaping organisms, or from perforation. The site of rupture is usually in the vicinity of the tumor, but at times distant from it, *e.g.*, in the distended cecum in a carcinoma of the rectum (Anschutz). Intestinal carcinoma is usually fatal before the end of the second year; Kraske says 4 to 5 years for carcinoma of the rectum.

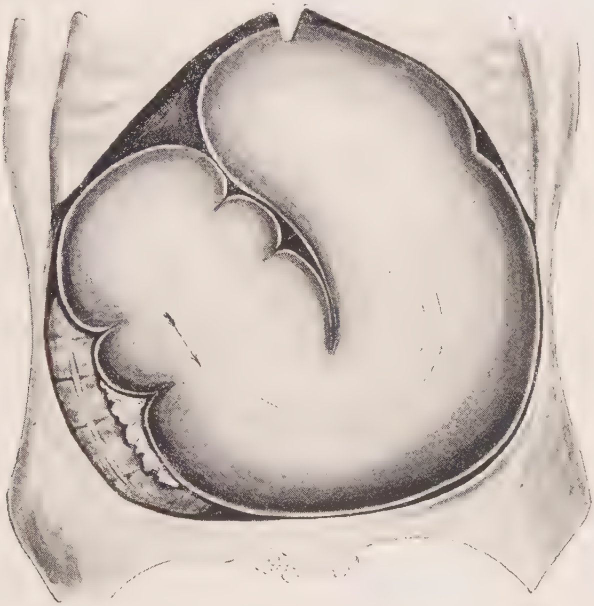


FIG. 391.—Abdominal aspect of immense dilatation of transverse colon with curving downward caused by a small constricting scirrhous carc. of the lower descending colon. To the right, down in the abdominal cavity, part of the ascending colon; part of omentum is visible between the latter and the immense transverse colon. Circumference of the opened and relaxed colon still 32 cm. (normally 15). The taenia visible in front is stretched to the breadth of 2.2 cm.; woman of 42 years; death due to perforative peritonitis. The opening of the perforation was posterior in the left hypochondrium and was caused by stercoral diphtheria. From a sketch made at autopsy.

Age of Patients.- Carcinomas of the intestine are rare in youth, but the author saw a stenosing mucoid carcinoma of the upper rectum with numerous metastases in a 17 year old girl; one of 19 showed a scirrhous cylindrical cell rectal carcinoma which had been diagnosed as a syphilitic stricture. Another 19 year old girl had a mucoid carcinoma of the sigmoid; a typical adenocarcinoma was found in a 19 year old male; indeed a 15 year old boy had a carcinoma of the colon (globocellular solid carcinoma) (cf. I.-Diss. of E. Bernoulli). They occur at even an earlier age (lit. by Sternberg, v. Muralt, Zuppinger, Lang, etc.). As a rule, however, they appear between the 50th and the 60th years. In a 95 year old man, the author saw a latent carcinoma of the cecum without metastases. Males are much more frequently the victims (with the exception of juvenile carcinomas). Among 1021 cases, Kuttner found 62% in males and 38% in females.

A carcinoma of the intestines and an independent second carcinoma in another organ are very rare. In such cases, the primary nature of both growths must be demonstrated by histological differences. In an 87 year old woman, the author saw a large, bowl-shaped, round cell carcinoma of the cecum which perforated into the duodenum and a small adenocarcinoma of the gall bladder (with two calculi); in a 74 year old man an adenocarcinoma of the rectum and a squamous cell carcinoma of the esophagus (cf. Schw. No. 10, 1906); in a 76 year old woman an adenocarcinoma of the rectum and a scirrhous carcinoma of the breast (solid scirrhous carcinoma) (cf. Schw. No. 17, 1906).

In rare cases, a carcinoma may develop in the vicinity or in the base of an old tuberculous intestinal ulcer (p. 802).

Metastases occur first in the peritoneum, then the liver (through branches of the portal vein), in the retroperitoneal lymph nodes, etc., but sometimes they are absent. In a 31 year old man, the author saw metastases of a carcinoma of the rectum in almost every organ. In a 73 year old man from whom a mucoid carcinoma had been removed 7 years before, the only metastasis was a polypoid, occluding, mucoid carcinomatous plug grown into the hepatic duct from the liver, causing fatal icterus (s. I. Diss. Rocco, Basel).

Infiltration of the serosa of the bowel including the appendix, (and also the other layers) may come from an intestinal carcinoma or other carcinomas primary in the stomach, uterus (or of the parametrium) ovaries, gall bladder, etc. These infiltrations form larger and smaller nodules, favor the region of the mesenteric attachment, constrict the lumen, or penetrate the bowel wall, cause multiple stenoses of the bowel without invading the mucosa. As the author saw in a 47 year old woman, one year after hysterectomy for carcinoma, a small hard carcinomatous infiltration in the transverse operative scar in the pelvic cellular tissue had annularly constricted the sigmoid, 25 cm. above the anal ring to the thickness of a catheter, with enormous dilatation of the colon, ileus (colostomy after complete constipation for 23 days) and final fatal peritonitis.

Secondary true metastatic carcinomas of the intestines are relatively rare. They occur (retrograde) by way of the lymphatics, or by implantation, especially in Douglas's cul de sac (Rosenstirn), or more rarely through the blood stream (Askanazy). They progress from the serosa, not rarely from an adjacent lymph node, into the wall and proliferate more freely as soon as the loose submucosa is reached (fig. 393). Hematogenous tumors are first located in the internal layers (mucosa and submucosa) as islands, or plaques with central umbilication (fig. 392), or as ring-shaped nodules producing stenosis. They may be single (fig. 393), or more often multiple, especially in the duodenum and jejunum, more rarely, lower in the ileum and colon, but do occur in the wall of the rectum where they suggest a primary stenosing tumor (van Dann described them—Douglas metastases; lit. by Schnitzler, Boas, Dittmer). But Douglas metastases may

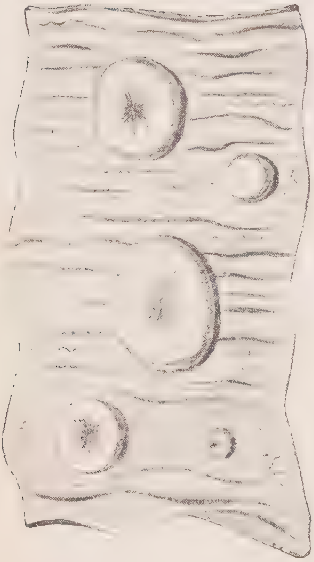


Fig. 392.—Multiple carcinoma metastases in jejunum with primary larcinoma of pharynx in man 62 years cod. ¾ nat. size.

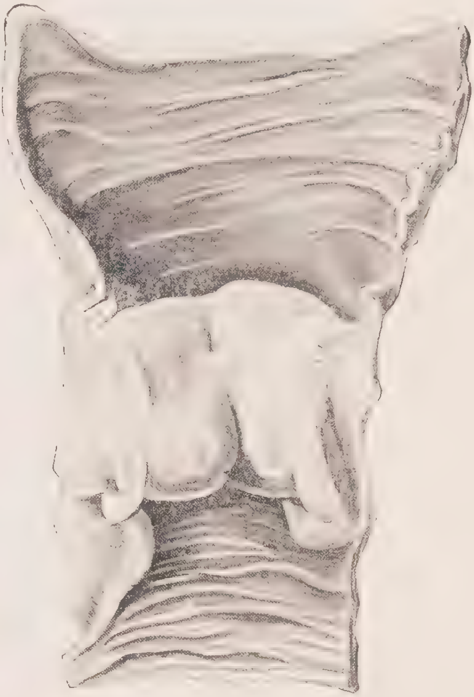


Fig. 393.—Stenosing metastatic carcinoma of ileum from primary horny carcinoma of uterus (extirpated 5 months before), 70 cm. above the valve of Bauhin; dilation of the bowel above; woman 47 years old; ¾ nat. size.

also reach the uterus (Heinemann). According to our experience, most of such stenosing metastases come from a gastric carcinoma, or still more frequently, from a carcinoma of the gall bladder (I. Diss. Schwietering). The metastatic carcinoma of the ileum in fig. 393 resembles a primary carcinoma. Such rare cases, with multiple hematogenous metastases in the intestines are usually part of a general carcinomatosis (O. Israel, Borrmann, and others). The author saw islands scattered (fig. 392) throughout the entire bowel of a 62 year old man, with general carcinomatosis from a very small primary tumor of the pharynx (left pyriform sinus); these unusual metastases took place in: brain, spinal column, tonsils, thyroid, lungs, abdominal walls, numerous peripheral lymph nodes (groin, axilla), spleen, kidneys, adrenals, pancreas, epididymis; none to the liver. Occasionally, regional metastases appear in the bowel wall in the vicinity of a primary intestinal carcinoma, or carcinomas develop in lower segments in conjunction with higher tumors. When secondary carcinomas ulcerate into the lumen, primary tumors are simulated.

Sarcoma.—Primary, ordinary sarcomas are rare as circumscribed bulging tumors, with partly ulcerating, partly smooth surfaces, the edges of which are covered by firmly attached smooth mucosa which is lost as the tumor grows (fig. 394). They are prominent, irregular or circular tumors, often circumscribed, especially those around the ileo-cecal valve, rarely polypoid, usually single. They occur at any age, even in childhood. Men are 3 times more frequently attacked then women (Westermark). Often, they can be differentiated from carcinoma only by microscopic examination. They are mostly round, sometimes alveolar, more rarely spindle cell tumors. Babes and Nanu, Ghon and Hintz, Kieckenberg, Demmin, v. Salis report so-called malignant leiomyomas or myosarcomas (histology under uterus); v. Bokay reported a giant cell sarcoma in a 9 months old baby. In a 38 year old man, the author saw a small, spindle cell sarcoma larger than a child's head which had both infiltrated the layers of the wall to the outside and had developed free in the lumen in the form of thick clumps; in a youth 19 years old, the author saw a perivascular spindle cell sarcoma the size of a child's head in the wall of the cecum; it was covered by mucosa, but had reached the lumen which it had distended and distorted. A rare polypoid melano-sarcoma with rounded angular cells the size of a cherry was seen by the author in a woman 59 years old; it had caused ileo-cecal invagination. Sarcomas develop in the submucosa, soon invade the muscularis mucosae, and usually avoid the serosa. The tumor tissue may undergo fatty, necrotic or hemorrhagic changes, but frank ulceration is rare. Stenosis may be absent, but is usually present. Even an aneurysmal dilatation may occur, if the muscularis loses its contractility and elasticity. Invagination is relatively

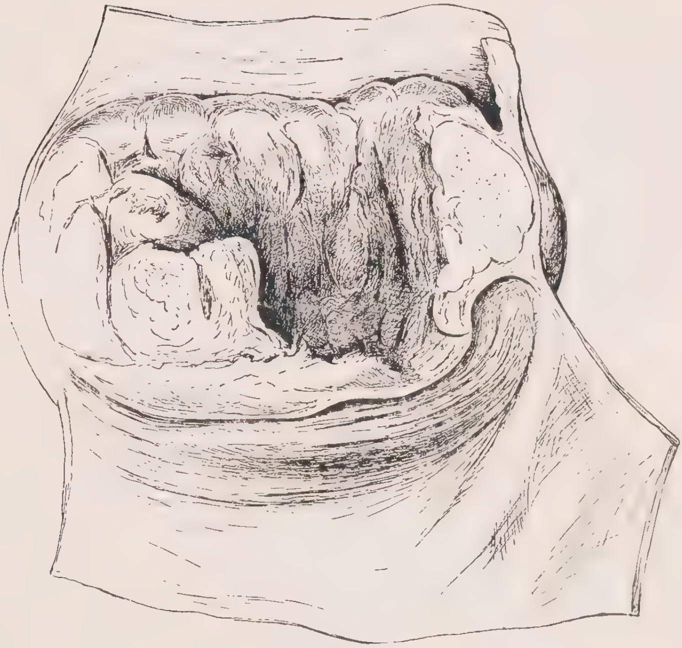


FIG. 394.—Round cell sarcoma of ileum of man 69 years old. Symptoms of stenosis 6 months before operation (v. Mikulicz) with weakness and loss of weight (23 lb.); ¾ nat. size.

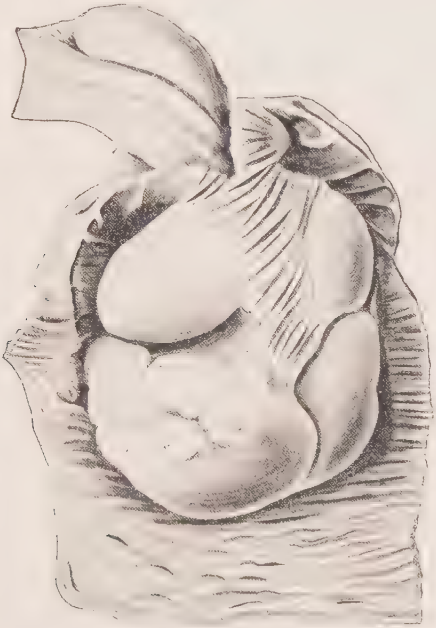


FIG. 395.—Invagination of the sarcomatous ileo-cecal valve into the colon. Above left ileum and above this the sarcoma; appendix. Round cell sarcoma with many mitoses in boy 5 years old. Metastases to lymph nodes, liver, peritoneum, lung, pleura, cerebellum; thrombosis of femoral veins; hemorrhagic infarcts, lungs; ½ nat. size.

frequent; metastases usually early. They are most frequent in the lower ileum (lit. by Rheinwald, Munk, Rademacher), and the cecum, especially the ileo-cecal portion (Goto), rare in the rectum (Key, Schumann, Lapeyre), the duodenum (v. Salis, lit.), and quite rare in the appendix (Carwardine, Harte); they may reach enormous size in the colon (man's head). The author described a very rare stenosing round cell sarcoma of the rectum with extensive invasion fatal in a few weeks, from invasion into the prostate, bladder and perineum (fig. 397); in a man 50 years old he saw directly above the anus, a rounded projecting tumor as large as a quarter with hard margins which looked macroscopically like carcinoma, but which microscopically proved to be spindle cell sarcoma (no metastases). In the lowest rectum and around the anus, melanosarcomas occur (Wiener, Schumann, Sandner). In a 55 year old man, the author saw a polypoid melanotic sarcoma of the rectum with elongated giant cells

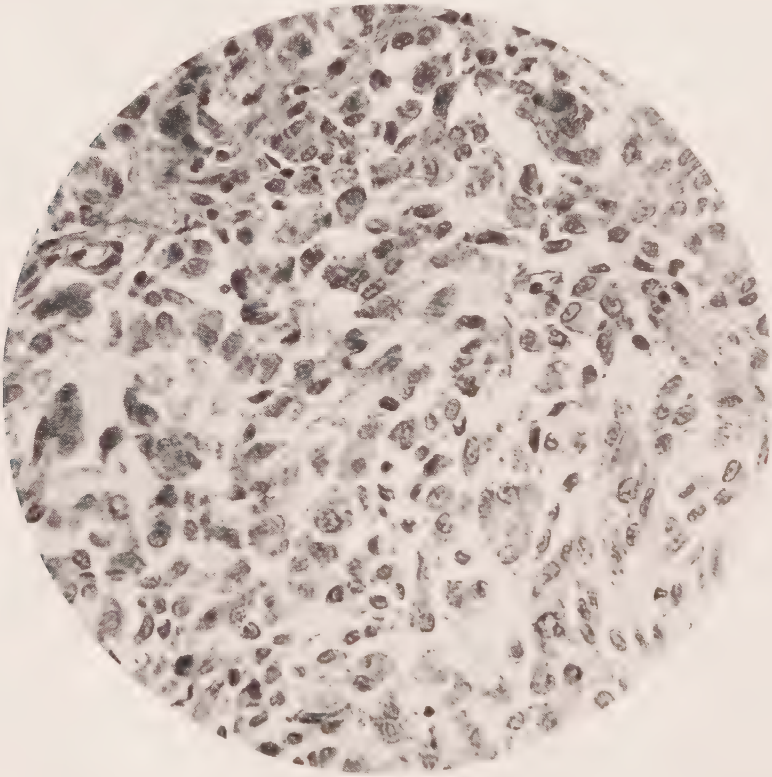


Fig. 396.—Spindle cell sarcoma of the rectum. This was in a man 38 years old whose trouble dated three months before operation. He had bleeding from the rectum, sense of fullness, some tenesmus and slight pain. The rectum was resected and a spindle cell tumor removed which was large, vascular, soft, easily bleeding, its main bulk being under the mucosa. It had not as yet extended annularly around the tube. Patient died eight months later of metastases to the lungs and other organs. × 300. L. H. #19779.

and other atypical, odd, partly pigmented cells. The melanosarcomas here or elsewhere are distinguished by great malignancy and early numerous metastases (all Marchand's cases). See p. 728 in reference to rare spindle cell sarcomas of Meckel's diverticulum.

Primary lymphosarcomas favor the small bowel (pp. 278 and 279), especially the ileum, and are rarer in the colon (lit. Glinski, Lecene), duodenum (lit. by v. Salis), and rectum. They spring from the adenoid tissue of the deep layers of the mucosa or submucosa, infiltrate large areas with white, glossy tumor masses to the thickness of a finger (Freud), or with lumpy masses, or broad based or pedunculated tumors, at times with plaque-like arrangements. They cause stenoses (comp. f. i., v. Haberer, Kroll), or invaginations (Fulci, lit.), or probably more frequently, aneurysmal dilatations of the rigid infiltrated, thick walled, sometimes ulcerated tube (rarely perforated, see Boehm, Madelung and others). The perioneum may show diffuse or nodular infiltration. The mesenteric nodes, when infiltrated, are usually markedly so. Distant metastases are numer-

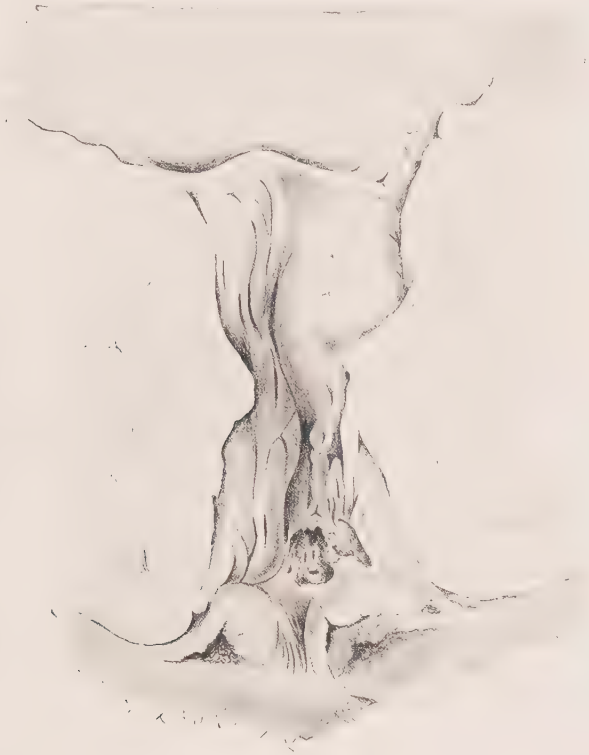
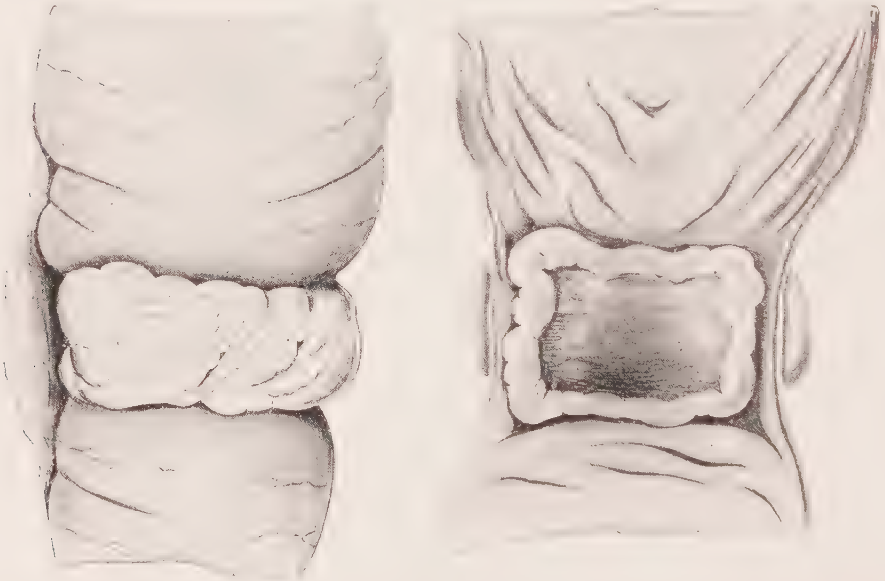


FIG. 397.—Immense, moderately stenosing round cell sarcoma of rectum, developed in but few weeks (!). Rectal mucosa infiltrated in rolls, smooth, below an angular ulcer. Periproctal tissue greatly infiltrated; the tumor masses bulge at the perineum hemispherically; they have been cut into the irregular granulating incision areas, right and left of the anus; man 30 years old. See text above. (Deutsche Chirurgie, No. 53, 1902); ½ nat. size.

ous and early (see observations on p. 279 of a man 25 years old). Primary multiple lymphosarcomas also occur (case 212). They have been observed both in children and in advanced old age (Schmidt, lit.). Sometimes fever is a symptom. In contradistinction to ordinary sarcomas, some lymphosarcomas cause no striking disturbances of general well being for a long time, but in other cases, the course is rapid (2 to 3 months); death is due to cachexia, seldom to perforative peritonitis. (See p. 806 for leucemia and aleucemic adeny.)



Figs. 398 and 399.—Secondary sarcoma of small bowel from sarcoma of pylorus; (l. illust.) from outside, a stenosing open ring; inside (r. pict.), an ulcer not quite circular, with margins which resemble primary carcinoma. Microscopically polymorph. and large round cell sarcoma with giant cells with large nuclei; 4/5 nat. size.

Secondary sarcomas, especially melanotic types, are more frequent than primary. Their situation is in the submucosa, muscularis or serosa; the epiploic appendages are often invaded, or nodules appear at the mesenteric attachment. Masses bulging into the lumen may cause stenosis, but they rarely ulcerate; when they do, they appear like primary tumors (carcinomas; figs. 398 and 399). The author saw such an infiltration in the upper jejunum from a round cell sarcoma of the thyroid gland in a 63 year old man; there was also a coin-shaped ulcerated infiltration in the stomach. Secondary lymphosarcomas are also relatively frequent (p. 279).

Diseases of Special Parts of the Intestines

Restricted localization is shown by diseases in (*a*) duodenum, (*b*) cecum and appendix, (*c*) rectum.

(*a*) The portion of the duodenum above the papilla of Vater (see topographical fig. 82, p. 140), has certain diseases in common with the stomach. Hemorrhagic erosions and round (peptic) ulcers with rare exceptions, are found only in this part of the duodenum where the gastric juice is still acid.

The ulcer, just below the pylorus, or 2 to 4 cm. distant and always in the superior horizontal portion, especially on the posterior wall (pancreatic side), or the anterior wall, is exactly similar to a gastric ulcer. Its edges are flat or slightly rolled up due to overhanging mucosa, the base is smooth and it becomes deeper by steps. Ulcers may be multiple, and may be due to embolism. If a larger embolus is driven into a vessel, the subsequent necrosis and ulceration are annular, since the vessels grasp the intestinal wall as in a fork. Sometimes two separate transverse ulcers are found, but they lie on a common line which encircles the bowel. Duodenal ulcers may become stationary, and thus latent. They also may undergo spontaneous healing by scar tissue. v. Hansemann claims he has never seen this occur. The author saw it twice in 22 cases (s. I. Diss. Wolowelsky, Basel, 1906); Mayo found healing in 82% after gastrojejunostomy. According to Hart (lit.) more than ½ of the ulcers have a tendency to heal quickly. According to Helmholz, superficial ulcers may be covered with epithelium from Brunner's glands. See literature by Melchior.

If the scar tissue causes stenosis (very rare), the upper portion of the duodenum is dilated, the pylorus stretched and insufficient and gastric ectasia results; severe subjective symptoms may also be caused by the periduodenal adhesions of older ulcers. Duodenal ulcers are much rarer than gastric ulcers, and more dangerous but they have little tendency to become carcinomatous; it was seen by the author in a 24 year old anemic man (cf. Mayo). In contradistinction to gastric ulcers, they are much more frequent in males than females, and indeed may even occur in the newborn (lit. by Roether). In such cases, Aschoff suggests that pressure might be exerted on the duodenal wall by adjacent organs, such as the liver and gall bladder forcing the duodenum against the head of the pancreas. Scagliosi (lit.) believes that pressure from adenoma-like, proliferating duodenal glands and accessory pancreatic rests, are responsible factors. The ulcer perforates quite frequently, twice as often when in the anterior wall, and is usually followed by general peritonitis (Collin, Pagenstecher). Sometimes when in the posterior wall, a local peritonitis develops before perforation takes place, and adhesions to the vicinity (liver, neck of gall bladder, pancreas), keep the duodenal contents from spreading and the result is a subphrenic peritonitis, essentially confined to the right hypochondrium, or a subhepatic, circumscribed, exudative peritonitis;

this may extend along the lesser curvature as far as the cardia. These are called "subphrenic abscesses," and often give rise to a secondary general peritonitis. In other cases, death occurs in 1 to 2 days after rupture. Quite often (according to Wanach, in half of the cases), a perforative peritonitis is the first symptom of the ulcer. Erosion of vessels is fatal, at times, by hemorrhage from the pancreatico-duodenal artery or its branches, the gastro-duodenal artery, very rarely from the aorta or portal vein. Sometimes two ulcers are present at the same time, for instance, one caused severe hemorrhage and the other fatal perforative peritonitis in a 3 year old girl observed by the author. Duodenal ulcers are relatively frequent in sepsis (1:37 according to Perry and Shaw), and are said to be frequent after burns of the external skin, although Marchand, Eug. Fraenkel saw none in 50, and 108 cases respectively. The author's experience agrees, but Gruber does not exclude the possibility of a causal rela-

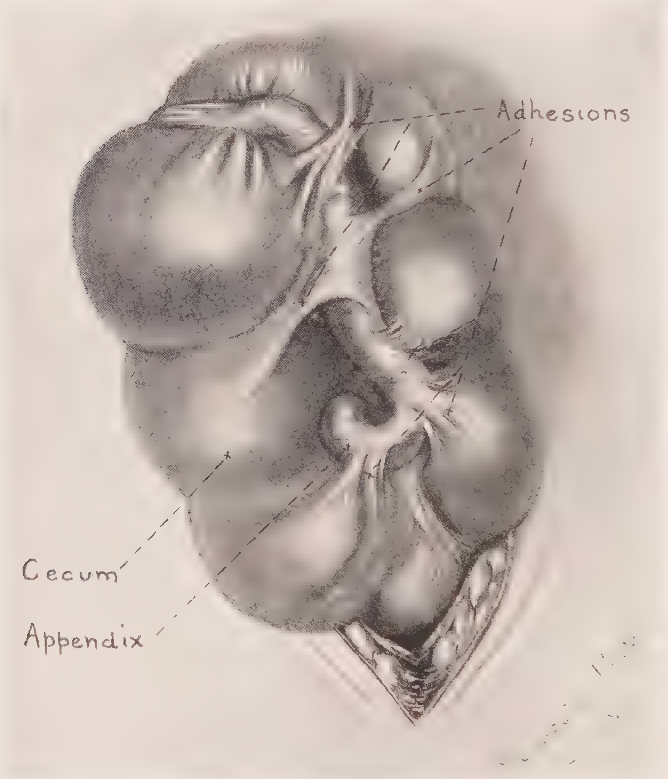


FIG. 400.—Retrocecal appendix.

tionship, which may be embolic, thrombotic and ecchymotic. Some think an embolic origin (retrograde) is especially important in appendicitis (Kummel); irritation of the vagus is supposed to initiate ulcers in the duodenum as in the stomach (Bode and Singer and others). According to Alvazzi, duodenal ulcers are relatively frequent in chronic lead poisoning as in house painters (Schiff). Direct trauma is a very rare cause of duodenal ulcer (Melchior).

Catarrh of the duodenal mucosa may spread upwards in the bile ducts, or by swelling obstruct the duodenal papilla; icterus (catarrhal or congestive icterus), stasis and congestion of pancreatic juice result. Some ulcers of the duodenum chiefly, carcinomatous, (fig. 480) which may be fungoid or infiltrating, are situated near the papilla and may produce stasis of bile (icterus) and pancreatic secretion, sometimes with ectasy of the common duct and gall bladder, and as in fig. 480, with fat necroses. They may also cause duodenal stenosis with dilatation of the stomach. (See lit. by Geiser; duodenal carcinoma, 9 cases from the Path. Institute, Basle D. Z. Chir. 86, 1906; Also Aynaud, Morian.) Adjacent lymph nodes, especially the portal, may be markedly infiltrated.

Scagliosi believes carcinomas come from proliferating duodenal glands and pancreatic rests, and are rarely preceded by an ulcer.

Carcinomas above the papilla cause symptoms similar to those of carcinoma of the pylorus.

It must suffice to point out that all possible "tumors" may cause duodenal stenosis such as circumscribed peritonitis, aneurysms of the aorta, hydronephrosis, renal, liver and mesenteric cysts, neoplasms of adjacent parts. See arterio-mesenteric duodenal ileus, p. 714.

See diverticuli (p. 749), congenital atresia, (p. 720), duodenal ankylostoma (p. 853), aberrant pancreas (under pancreas).

(*b*) **Colon, Cecum and Appendix.**—Inflammations of the cecum, typhlitis, are of slight importance compared to those of the appendix. They may result from fecal retention in chronic constipation (stercoral typhlitis), from firm hard fecal masses (scybala), or foreign bodies such as seeds of fruit, which distend the cecum, or intestinal worms (Schiller and others) all of which cause more or less irritation of the mucosa. Appendicitis may be present at the same time. The inflammation due to bacteria and their toxins runs a chronic catarrhal (phlegmonous) or necrosing diphtheritic course (stercoral diphtheria); it may lead to multiple ulcers, inflammation of the neighborhood (perityphlitis, pericolic adhesions), abscess formation and perforation (Cordes, Ropke, Hagenbach, Cramer, Fahr).

Chronic colitis especially of the cecum and ascending colon may cause the so-called inflammatory stenosing ulcers of the colon, easily mistaken for malignant neoplasms (Tietze, lit.). A somewhat similar condition is diverticulitis of the sigmoid (p. 749; Sudeck). Typhlatony or dilatation of the cecum (Fischler) is a clinically not unimportant chronic dilatation which is caused by various conditions, *e.g.*, periodical upward displacement of the movable cecum, angular kinking due to a very short mesentery and fixation of this kink by pericolic adhesions perhaps due to trauma of the abdomen (Brosch).

Specific ulcerative processes (tuberculosis, typhoid, dysentery) as already mentioned, frequently involve the cecum. Paschkis reports hemorrhagic necrosing typhlitis in "la grippe." Tuberculosis especially produces voluminous or smaller, firm, stenosing tumors in the ileocecal region (Conrath, Fibiger and others). This is spoken of as the hyperplastic form of stenosis of the bowel in contradistinction to the simple cicatricial form (details, p. 801).

The appendix is frequently the seat of severe bacterial inflammations; it is the chief location of fecal calculi (p. 846); it often produces severe secondary changes.

Congenital absence of the appendix is very rare (p. 720). Diverticuli are among the rarest of rarities (Hedinger, Sturm).

See Peter in reference to the function of the appendix.

The appendix, on account of its length (6–8, 10, rarely to 25 cm.; it grows to the fourth decade), narrowness and cul de sac is almost predestined to retention. A very short appendix is quite rare, but the author saw one 2.5 cm. in length with a wide funnel shaped opening in a boy 13 years of age. This is sometimes helped by a valve-like fold of mucosa at its entrance, the valve of Gerlach (see v. Hansemann, and in opposition, Oberndorfer). When peristalsis is normal the muco-fecal contents (meconium in the fetus) are constantly discharged. The assertion of Oberndorfer that feces as contents of the appendix are pathological is contradicted by the experience of others. But retention is assured with insufficient peristalsis, or stasis in the cecum in chronic constipation (feces and gases) or in consequence of excessive length, irregular position (emphasized by H. Albrecht and Liertz), or kinking (Klauber) or stenosis due to swelling of the mucosa in intestinal catarrh, or obstruction from fecal concretions, etc. In all these conditions the contents of the appendix necessarily stagnate and this always causes increase in number and virulence (Lanz and Tavel) of the bacteria present. These are streptococci, pneumococci, staphylococci (Haim, Franke and others), colon bacilli and anaerobes which produce powerful toxins of inflammation and suppuration (Runeberg, lit. Heyde). Stagnation, as in the bile ducts, is thus very important in the development of inflammation. The question of the importance in appendicitis of the frequent animal parasites has been discussed for many years; most authors are inclined to consider them unimportant, but others, such as Blanchard, believe they may help in the entrance of bacteria (Wilson, Cecil and Buckley). Lately, Rheindorf in extensive investigations, assigns an important part to parasites, especially to the oxyuris; he emphasizes lesions of the epithelium and the mucosa (tunnelling) as effects of oxyuris and believes they may be portals of entry for bacteria. Reinhardt and Lawen also recognize epithelial lesions by which oxyuris favors bacterial infection (Goldzieher); but oxyuris alone packed in the bowel may simulate acute or chronic appendicitis. That oxyuris and other intestinal worms (trichocephalus and ascaris, see Schloessmann) may cause symptoms similar to appendicitis, especially in children, is well known, even though this pseudoappendicitis reveals no lesions in the removed appendix (Sagredo, Hueck, and others, fig. 401). Aschoff, however, opposes this conception of Rheinsdorf, and states that his "oxyuris lesions" are artefacts (characteristic defects said to be caused by oxyuris, and remaining even when oxyuris is no longer present). Rheindorf confidently maintains his opinion; at any rate, the question requires more investigation, and when diagnosed, oxyuris should be properly treated. Autochthonous fecal

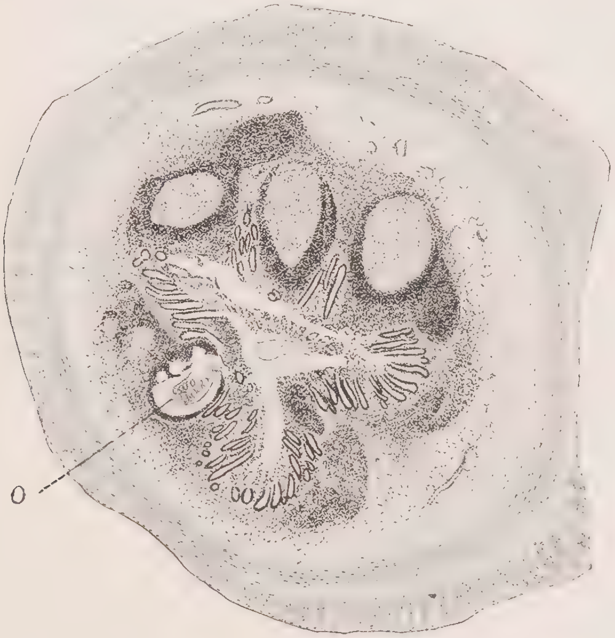


Fig. 401.—Appendix without inflammatory changes containing an oxyuris (O); its ova are recognizable in a smooth crypt. A piece of oxyuris in the lumen in which also a portion of the mucosa is suspended (artefact). In the lymphoid tissue 3 (lighter) germinal centers. Removed at operation. (Low power.)

concretions, the relatively rare foreign bodies, included in the center of coproliths, and free foreign bodies, are all of some importance. Fecal calculi are concentric deposits of mucus, perhaps with salts of calcium and magnesia, around pure fecal nuclei. Lamellated mucous masses may in corporate fecal matter, become encrusted and form stony concretions. According to v. Brunn, many fecal concretions consist chiefly of bacteria. The fecal concretion is often located in a circumscribed dilatation of the lumen. Actual foreign bodies (2a) as nuclei of fecoliths are much rarer; they are usually insoluble materials such as hair, bristles, wood fragments, splinters from agate-ware, insoluble vegetable particles from food, a fish bone, small shot, fragments of a needle, gall-stones, fruit seeds smaller than a cherry stone, etc., (lit. by Kelly, Rebentisch, Oberndorfer, Retzlaff). They are in the centre of soft fecal masses and become more or less encrusted by calcium phosphates or triple phosphates. If incrustation is very marked, the hard, laminated calculi may be mistaken for fruit seeds. But small, simple fecal concretions are usually not hard, but dense, relatively dry, light in weight, oval or cylindrical and rarely larger than a bean. (The author saw one 3 cm. long by 1.7 cm. thick, see lit.) Even faceted calculi have been observed. Enlargement usually occurs by additional deposits of mucus, until they are much larger than the entrance to the appendix. The brown color is derived chiefly from bilirubin, especially hydrobilirubin. The more calcium, the lighter the color. Free foreign bodies are rare, such as needles (v. Hansemann), sand grains, shirt buttons, fruit seeds, etc.

Appendicitis, more topographically peri- or epityphlitis, is very frequent and occurs at all ages. According to Petren, the danger of appendicitis decreases after the 30th year. Appendicitis or epityphlitis is anatomically-topographically not a sharply defined conception, since the length of the appendix (p. 832) and its position (hanging into the pelvis to the outer side of the cecum, behind or on it, upward or downward from the cecum, in a hernia, etc.) are variable (lit. by Fiedler, Sitzer and Liertz).

There are two main theories as to the development of appendicitis (see lit. in appendix).

Enterogenous Origin.—This is the older and more logical idea; the author cannot help embracing this in the great majority of cases. The pathological processes are essentially the same as in inflammations else where in the bowel (p. 758 a.ff.), but modified by the special anatomical conditions such as narrow appendiceal cul de sac with a mucosa rich in follicles and crypts, etc.

According to the investigations of Aschoff and his school, the inflammation begins in one, or several crypts of the mucosa as collections of leucocytes below the epithelium; a minimal defect of the epithelium is said to be always present containing a plug of leucocytes and fibrin. This is the so-called primary defect, which, according to Goldzieher, may be present anywhere in the mucosa. From this there quickly develops the phlegmonous stage (the catarrhal appendicitis of Sonnenburg, Franke) by confluence of numerous wedge-shaped leucocytic foci which reach to the serosa, on which is deposited a fibrino-purulent exudate (toxic-abacterial). This may be complicated by minute intramural abscesses which perforate externally or internally and which may dissect the submucosa. Healing usually follows. But the phlegmonous stage may pass into the more severe ulcerative form, in which the primary defects enlarge into ulcers; this is almost always combined with fibrinous exudation and purulent secretion from the ulcer surfaces. This form may be complicated by ulcerative perforation and necrosis of the wall, due both to toxins and to arteritis and phlebitis, really an anemic necrosis or a hemorrhagic infarction. The dead wall becomes gangrenous and decomposed. Quite broad perforation may result. If healing takes place and the dead tissues are cast off, the reparatory proliferation results in adhesions and cicatricial obliteration.

Goldzieher differentiates: I. phlegmonous appendicitis—the severe form which causes the acute attack and corresponds to Aschoff's presentation by beginning in the depth of the crypts; II. superficial appendicitis, due to mild virulence of the bacteria; this shows three subtypes: (*a*) superficial catarrhal appendicitis, leucocytes invade the epithelium which is lifted into vesicles, and the surface mucosa is infiltrated with leucocytes. These are chiefly chronic cases and masked forms; (*b*) appendicitis superficialis exulcerans, a suppurative ulcerative inflammation; (*c*) superficial hemorrhagic appendicitis. (The author considers this classification useful in reference to the degrees of appendicitis, and for microscopic diagnosis.)

Hematogenous, Metastatic Origin.—According to the investigations of Adrian, Kretz and others, a metastatic origin is also possible, at least as an exception, even though Ghon and Namba dispute the conclusions derived from the animal experiments of Adrian and Jedesco (lit. by Canon, lit. in appendix to p. 834). According to Kretz, in acute angina, and inflamed lymph nodes of the neck, organisms, chiefly streptococci, enter the blood and become localized in the subepithelial follicles of the appendix, where he demonstrated follicular vessel embolic mycosis. This is succeeded by death of the vessel wall, hemorrhage into the follicles and their necrosis. Destruction of the cocci may occur with influx of leucocytes, with expulsion of the follicle and exudation of fibrin, or the condition progresses to a phlegmon.

In reference to the relative frequency of hematogenous and enterogenous origins, most authorities agree that the latter is far more frequent, and as Oberndorfer, among others, emphasizes, it is indeed difficult to understand why emboli should select the follicles of the appendix and under the same conditions not the equivalent follicles of the rest of the bowel (see lit. in appendix to p. 834).

Beitzke assumes there is a combined enterogenous, metastatic origin; the beginning is decomposition of the secretion of the appendix. Leucocytes, which pass from the blood into the injured mucosa, contain uninjured bacteria from the angina or other infection which are thus carried into the tissues and produce the inflammation. Exceptionally, an appendiceal phlegmon may have its origin via the lymph channels from a peritonitis (Sugi, lit.).

The effect of trauma in appendicitis is adjudged very differently. It is certain that it may be harmful to an acute process, and probably may cause recurrence in an older process (lit. by Bruning, Oberndorfer and Tiegel, Sonnenburg, Albu).

Recurrences, which occur in about ½ of the cases, represent new infections; the anatomical changes are similar to those of the first infection. If cicatricial stenoses are left from former conditions they favor localization in the part behind the stenosis. Delayed healing may be due to areas of distal fusions and collections of exudate, or to fecoliths. According to Aschoff, there is no such thing as a primary chronic appendicitis, but others believe there is (Goldzieher and others, v. Rosthorn); in spite of many anatomical investigations, no satisfactory correlation with the clinical symptoms has been achieved (cf. Kummell). See p. 840 in re chronic appendicitis.

Small, locally formed fecal concretions are viewed in various ways. They are considered harmless in themselves or even protective to the mucosa (Aschoff). Although possibly not the actual cause, Sprengel found them in 50% of cases of appendicitis, and Heile, and later Goldzieher, believe the occlusion which they sometimes produce is a factor in causing an acute attack. They only occasionally cause pressure atrophy of the mucosa with flattening of the follicles and crypts and thus a locus minorae resistentiae and are often found in histologically normal appendices, but, on the other hand, there can be no doubt that they cause complications in the severer form of appendicitis. Wherever they lie, they may (*a*) produce local disintegration of the mucosa by suppuration or decubital gangrene, because of their bacterial content, and their hardness; or (*b*) produce necrosis of the wall subsequent to thrombotic processes in the appendiceal mesentery; or (*c*) if the calculus itself has not caused ulceration it may prevent healing, and thus prolong the inflammatory process (Noll). Ulceration and perforation follow; the fecal calculus is present at the opening or is forced out and found usually near the point of exit. Where the ulceration is more marked, there are abscesses in the wall of the appendix which may rupture externally. Exudate behind the concretion may sometimes force it into the cecum and then the appendicitis subsides. (*c*) The calculus may act like a cork and prevent evacuation of contents, chiefly exudate collected distally; this stretches the walls and produces tension necrosis (p. 752) and perforation (fig. 402). Klemm agrees with our conception of appendiceal concretions and Aschoff also now acknowledges their importance. Consult Winkler, Rahm, (lit.).

If the inflammation spreads to the serosa, not necessarily through a break in the wall, a painful peritonitis develops (periappendicitis) of extent and degree depending upon the intensity of the primary process. This exudate may be minor and disappear completely, or there may be recurrences with organization of the fibrinous exudate until the appendix is swollen to the thickness of a finger and the adjacent tissues are covered with connective tissue adhesions, vascular at first, but later pallid (plastic appendicitis). This may cure the process, or it again flares up, *e.g.*, from occlusions of the lumen by adhesions, or loosening of adhesions and escape of a bottled up exudate. Even a suppurative exudate may be absorbed if it is well encapsulated between adjacent parts (loops of bowel) which have been firmly united by a productive peritonitis. Spontaneous healing also occurs when an encapsulated abscess ruptures into the bowel (auto drainage). But dense, fibrous, firm adhesions are remnants of the process. When an appendicitis has completely subsided, the organ may be partially or totally obliterated and changed to a cord or tape-like cylindrical or flattened strand of connective tissue without a trace of lumen.

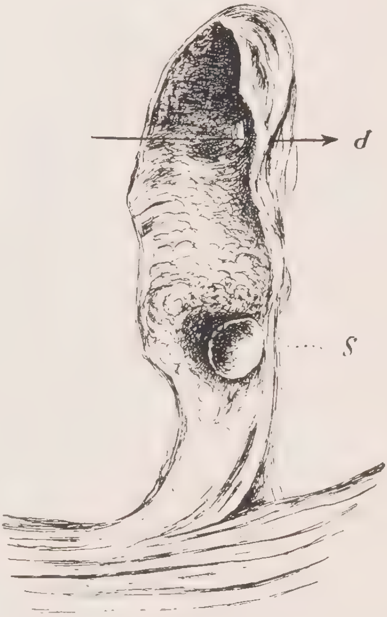


FIG. 402.—Perforation of appendix; s, occluding calculus in proximal part with surrounding gangrene of mucosa. Distally, distension gangrene with one perforation (p), see arrow. 16 year old girl, death perforative peritonitis; 9/10 nat. size.

In other cases, the local peritonitis becomes general in extent from rupture of the capsule of an abscess, *e.g.*, subsequent to trauma, concussions, cathartics, etc.

The local focus is called a "perityphlitic tumor," palpable through the abdominal walls; it consists of accumulated fecal masses in the cecum, swollen parts of organs and adhesions enclosing exudate.

Perforation produces a general suppurative peritonitis if no protective adhesions are present; if perforation takes place not into the abdominal cavity, but into adhesions, an intraperitoneal fecal abscess is the result (abdominal abscess), *i.e.*, a chronic, purulent, suppurative, encapsulated perityphlitis.

The perforated appendix may take on many appearances. Sometimes it is completely separated from the cecum, often only a piece of the distal end is found which is thick, still patulous, or obliterated. Sometimes no trace is found of the appendix in the foul smelling pus, or it breaks into thin-walled, friable necrotic fragments, or is wide open as though cut open, and covered within with ulcers and necrotic areas, or it is phlegmonous, or it shows numerous smaller or larger gaping holes, or is perforated like a sieve. Such massive destruction is sometimes due to lymphangitis or thrombophlebitis of its mesentery. But the thickened appendix may be well defined and show but a single hole the size of a mustard seed to a pea. The cecum may also be ulcerated.

If rupture occurs posteriorly into the loose cellular tissue of the right iliac fossa, the phlegmonous perityphlitis may assume enormous proportions (extraperitoneal fecal abscess). It may spread in the subperitoneal connective tissue upward as far as the kidney (paranephritis), liver and diaphragm (subphrenic abscess), to the pleura, and may, although rarely, even penetrate the diaphragm into the lungs. Downward, the process may extend to the perineum, the tuberosities of the ischii, or to the scrotum; in other cases, it points in the abdominal walls, or into the mesentery.

A paratyphlitic abscess sooner or later perforates somewhere into the peritoneal cavity, in women from an abscess in Douglas's cul de sac (Rotter), through the skin of the abdominal walls, into a hollow organ such as the colon, rectum, bladder, vagina, even into the gall bladder (Tanaka, lit.); thus an abscess may even heal (rarely).

Perityphlitis in women has the distinction of often posing as a tubo-ovarian tumor, because continuation of the inflammation to the adnexa and to the parametrium is very frequent (especially to the right side) (Moritz). The reverse also occurs. Propagation is by way of the retroperitoneal connective tissue to the pelvic floor, or through the suspensory ligament of the ovary; contrary to former statements, there are no special anastomoses between the blood and the lymphatic apparatus of these organ systems, and the so-called appendiculo-ovarian ligament, formerly considered important in the transmission of infection, is an inconstant and unimportant peritoneal fold. Formerly, appendicitis was considered rare in women, but now it is estimated as about 40% (Hermes) of the cases; indeed, according to v. Rosthorn, the disease is of equal frequency in the sexes. The primary disease is sometimes difficult to diagnose even at the post mortem, especially if the condition is old and accompanied by cicatricial changes of the pelvic connective tissue, peritoneum and adhesions.

Thrombophlebitis of the roots of the portal vein, especially the superior mesenteric, is a dangerous complication, and may cause embolism into the liver, continuation to the portal vein itself (pyelothrombosis), multiple abscesses of the liver (Zauleck, Weil) and peritonitis. Subphrenic abscesses often originate from appendicitis; the route is: veins, lymphatics, subperitoneal cellular tissue, peritoneal cavity (Piquand; good summary by Kovacs).

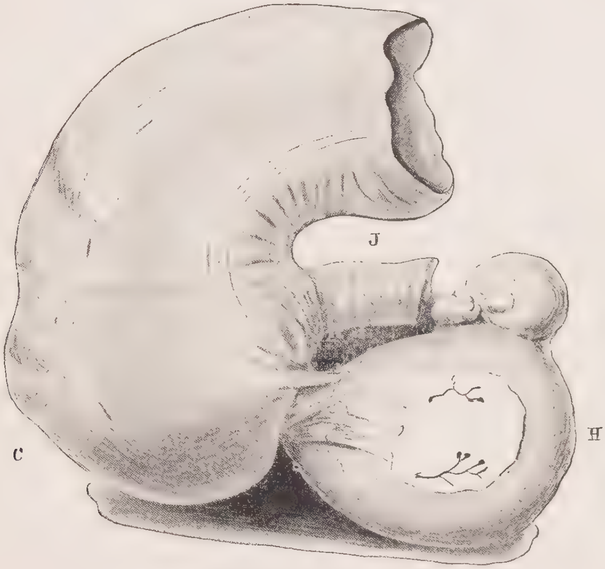


FIG. 403.—So-called hydrops, size of a fist; mucocele of appendix. H, oviform sac with small spherical diverticuli, corresponding to the distal end. Contents thick muco-gelatinous, gray white. C, cecum; J, ileum. 74 year old woman; about ½ nat. size.

If the distal portion of the appendix is free from fecal matter, or if it is closed from the proximal part, or if the whole appendix is closed to the cecum, retention of secretion and pear-shaped dilatation take place. If the contents are merely a muco-serous or thick gelatinous secretion, it is spoken of as hydrops, or better, mucocele, but if purulent, it is empyema of the appendix. These dilatations may be partial like diverticuli, *e.g.*, the peripheral parts, or universal, and with the thinning of the wall they become as large as a fist to a child's head (Nash). In rare cases, the contents assume the form of small gelatinous globules, often very numerous (Cagnetto) derived from cystic glands; it has been called by v. Hansemann "myxoglobulosis of the appendix" (Sturm, Schlagenhaufer, Pohl, Lignac, lit.). Eug. Fraenkel saw a case in which the mucocele had ruptured, evacuating its gelatinous contents into the peritoneal cavity

(Oberndorfer, Tomita, and under peritoneal pseudomyxoma, p. 880). Secondary diverticuli may bulge from the sac (fig. 403) (see v. Brunn and also Sissojeff, who mentions cystic diverticuli and small cysts springing from parietal abscesses; congenital diverticuli on p. 749).

The rather frequent, partial, more rarely total, obliteration of the appendix, especially of older individuals, is supposed to be simply an involution process in a "rudimentary organ" (Ribbert, Zuckerkandl, Sudsuki, and others), but this can not always be true (consult W. Muller, Berry and Jack, and others); it is true, however, that lymphoepithelial apparatuses cease to function in advanced age (Peter). Statements vary greatly as to the frequency of obliterating processes. Noll claims that it occurs in almost ½ of all adults, and Tomita states they are "enormously frequent." On the other hand, in the material at Basel, the author found in 733 males of all ages only 8.06%, in 731 females only 11.31% with obliteration. Among 100 men in the 5th decade, there were 11, and of 80 women, 9, in the 8th decade among 94 men, 10, and of 97 women, 24. But of 402 males and females in the 2nd, 3rd and 4th decade, there were only 11 individuals who showed partial or total appendiceal obliteration (s. I. Diss. Sitzer). Indeed, the fact that these changes are found frequently enough in younger individuals, as surgical evidence, is a testimony that it was due to an acute appendicitis which had run its course (Bierhof, Fitz, Faber, Ribbert's 2nd statements, Aschoff, Oberndorfer, Maaloe, Bolognesi; for the majority of the cases, also Goldzieher). That this appendicitis must be acute is also demonstrated by defects in the muscle which are surely remains of inflammatory scars (Mundt-Aschoff). These may lead to the formation of diverticuli (see Schweizer, Reiss, Konjetzny). But a number of recent investigators believe that some of the cases are due to an obliterating chronic appendicitis (Maaloe, Oberndorfer, Miloslavich and Namba), and Scheel differentiates 3 forms of chronic appendicitis: (a) granulating: granulation tissue fills the walls, probably derived from acute inflammation; (b) lymphoid form, hypertrophy of the lymphoid tissue; (*c*) chronic form; atrophy of mucosa and formation of connective tissue, chronic from the beginning or the result of acute inflammation. Goldzieher also recognizes a chronic inflammation of the appendix.

Specific ulcerative changes (tuberculosis, Winkler and p. 801, typhoid fever, dysentery, almost exclusively amebic, actinomycosis), also occur in the appendix and may give the symptoms of perityphlitis. Perforation is not rare in tuberculosis. The firm tumors of actinomycosis, usually difficult to define the borders (p. 803 and lit. by Winkler), occasionally look like fibrosarcomas, *i.e.*, hard and circumscribed, like true tumors (Hofmeister, v. Beck).

Primary carcinoma of the appendix on p. 816 and p. 817. Secondary infiltration of all layers of the wall may start from a secondary peritoneal carcinomatosis, see p. 823. See Askanazy in reference to sclerosing periappendicitis simulating carcinoma. In reference to participation of the appendix in diseases of the peritoneum, see Sugi; for gynecological disease (suppurative salpingo-oophoritis, ectopic gestation, pedunculated twisted cysts, etc.) see Nurnberger.

Rectum.—Atresia ani was discussed on p. 723, prolapsus of the rectal mucosa and complete prolapse on p. 745.

Simple inflammation of the rectum, proctitis, appears in acute and chronic forms. The first shows hyperemia and marked secretion, sometimes purulent, *e.g.*, gonorrhea. Chronic catarrh, frequently due to venous congestion or fecal retention, may lead to fibrous atrophy and slaty pigmentation of the mucosa, especially around the follicles.

Ulceration in the rectum may be caused by retention of feces, especially in women, in whom it often extends far enough to produce suppurative periproctitis and peritonitis. The author saw an ulcerated rectum dilated to the size of a child's head. Ulcers also occur in follicular catarrh, gonorrhea, diphtheria (also at the anus in children), tuberculosis, typhoid fever (rare), trauma, *e.g.*, poor technique in giving an enema (on the anterior wall), from drains (after extirpation of the rectum), from foreign bodies, syphilis in every stage (p. 802), suppurating hemorrhoids and tumors. Any one of these processes may lead to periproctitis. Bierende (Roessle) designates as postoperative proctitis and colitis a special form, observed with postoperative intestinal paralysis which he thinks due to paralysis of capillaries and stasis which cause nutritional disturbance of the mucosa and lead to necrosis and inflammatory exudation—formation of spotted, cloudy coatings. It is followed by loss of surface substance.

In reference to dilatation of the rectal veins—hemorrhoids, see p. 165. On section they reveal smooth-walled cavities or a tumor-like cavernous structure (p. 165). Thrombosis is common, and if present for a long lime, there is organization of the thrombi. Thus there appear soft fibrous nodules, consisting of vascular connective tissue. It may happen that these fibrous masses enlarge like tumors and then become very hard. Hemorrhoids may rupture, or inflammatory changes ensue in the walls from the chemical action of fecal matter retained in the mucous folds after defecation (v. Lenhossek). Thrombophlebitis follows eventually. The latter, and also simple thrombosis and perhaps embolism (into the lung or liver) have been observed after surgical removal. Inflammation of hemorrhoids may cause periproctitis.

Anal fissure is common in the presence of hemorrhoids; this is a small ulcer shaped like a myrtle leaf, flat and red and parallel to the anal skin folds. But it also occurs independent of hemorrhoids, especially in women, and is considered due to congestion of the anal mucosa, and therefore increases in its extent, with irritation from the passage of hard fecal masses. Since an anal fissure bleeds easily, and since congestion of the mucosa is often present, it is easily mistaken for hemorrhoids. They are extremely painful and cause reflex spasm of the anal sphincter.

Inflammations of the rectum (proctitis) extending to the loose connective tissue (the lower part of the rectum has no peritoneum) produce a periproctitis which may extend to the peritoneum and cause peritonitis. If due to a ruptured ulcer, as from impaction of feces, or more frequently, to tuberculous or carcinomatous processes, the periproctitis becomes suppurative. But it often leads to chronic cicatricial induration, most frequently in conjunction with syphilitic ulceration of the rectum. The suppurative periproctitis may produce irregular cavities from which fistulae lead off into the vicinity (rectal fistulae).

A fistula in the periproctal tissue is known as internal incomplete (fig. 404); if it ruptures into the rectum, it becomes complete internal; if it opens outward in the vicinity of the anus, it is complete external (a in fig. 404). Tuberculous fistulae often produce extensive ulceration in the skin of the anal region. If a fistula heals above, and no longer communicates with the rectum, it is called external incomplete.

The author saw a very rare actinomycotic peri- and paraproctitis in a 38 year old driver of a horse car. Clinically, it was diagnosed as carcinoma of the rectum. At autopsy, the rectum was surrounded anteriorly and laterally by a contracting cicatricial tissue as thick as a thumb, which, filled with cloudy-white friable, partly puriform foci and fistulous tracts, formed a tumor as large as a small fist; it had grown into the prostate, seminal vesicles and the posterior bladder wall. No lesion was present on the internal rectal surface (or the rest of the bowel), the urinary tract, or elsewhere in the body. It was possibly an intestinal infection or better, an external infection of the anus, similar to the case of Popow, in which the patient used straw or grass to cleanse himself after defecation. In other rare cases of this type, the infection resulted directly through a lesion in the mucosa or through a foreign body injuring the skin in the anal region (Poncet and Thevenot, lit.).

Primary suppurative periproctitis occurs occasionally in pyemia, puerperal sepsis and typhoid fever without ulceration of the rectum.

Chronic ulcerative stenosing proctitis and periproctitis as a disease is not uniform in etiology, but probably is due in most cases either to syphilis or gonorrhea of the rectum; it occurs almost exclusively in females (fig. 404).

It consists of the formation of thick, rolled, shelf-like or folded elevations, often longitudinally parallel, and of strands of scar tissue which pass through ulcerative defects with smooth floors and sharp edges, and which reach to the muscularis and occupy the entire upper part of the rectum. In rare cases, the ulceration extends higher, as far as 32 cm., or as the author saw in another case, 56 cm. Indeed, in a 36 year old woman with dry caries of the skull, and scars on the palate, the author saw the whole colon, which was shortened to 1 m. in length, occupied by a connected smooth ulcer. In such a case, it must be called "stenosing colitis" (similar to a very rare dysenteric stenosis of the colon, p. 774). Above, the ulcer is demarkated from the healthy mucosa by a jagged line. The part of the rectum ulcerated is usually markedly stenosed, sometimes extraordinarily shortened (p. 812), and dilated above. The muscularis, and also the periproctal tissue, are often considerably thickened (fig. 404). The rectum, with rare exceptions is firmly adherent to its vicinity and is not displaceable; its wall is partly undermined and perforated by fistulae and wide openings. Fistulae lead from the periproctal tissue to the perineum, to the vagina and vulva, rarely to the bladder and still more rarely to the abdominal cavity. In most instances, elephantiasis-like prolifera-

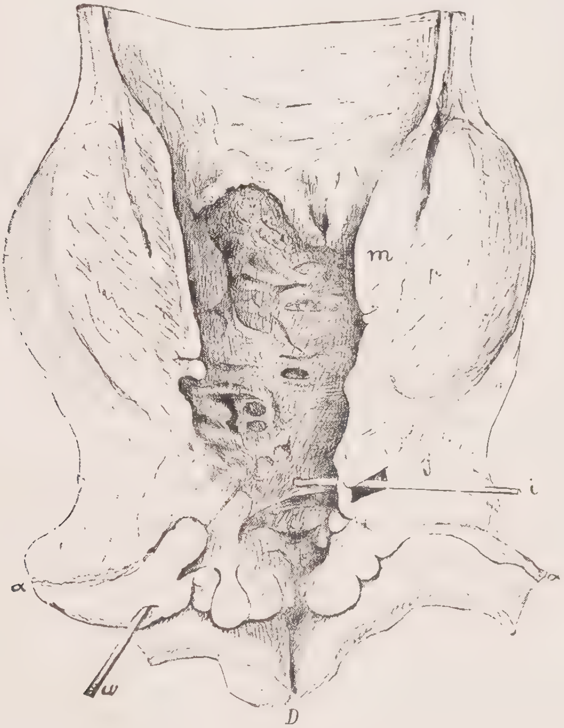


Fig. 404.—Chronic ulcerative and stenosing proctitis and periproctitis in a syphilitic woman; m, rectum cut open, muscularis thickened; p, cicatricial periproctal tissue; D, perineum; a, outer complete; i, incomplete rectal fistula; a and a are corresponding areas; ½ nat. size.

tions occur, the labia majora are thickened to firm rolls, and around the anus are condyloma-like, pedunculated excrescences (fig. 404) which block the anal opening. On these hyperplastic new formations, torpid ulcerative destruction may be established. The anal ring itself is very often free from ulceration, but the rectal mucosa is prolapsed and studded with hemorrhoids; in fact, some of the elephantiasis-like nodules on the anus are hemorrhoids undergoing fibrous change. Amyloidosis of the internal organs is not rare. Perforative peritonitis may come from the dilated bowel situated above, usually from stretching or decubital necrosis in coprostasis, more rarely, as in a case of the author, from perforation of a parietal abscess.

Etiology.—This affection occurs almost exclusively in females, very often in prostitutes with previous syphilitic and gonorrheal histories. Opinions are divided in reference to the nature of the condition. Some of the cases are syphilitic (1) rarely in the earlier stages (primary infection or ulcerated papules of the rectum; discharge of specific vulvar secretion), more commonly in tertiary stages in which mucous and submucous gummas disintegrate into ulcers with their consequences, especially stricture. Congenital late syphilis is included (Lewin; Goebel).

This is doubtless correct in many cases. Absolute proof of this origin is naturally possible in very few cases, since the changes are seen, as a rule, in such an advanced cicatricial stage that the autopsy gives neither local nor other organic findings of positive lues. According to Rieder, advanced diffuse alterations in the veins (peri- meso- and endophlebitis) with productive lymphangitis in all stages both in the perirectal tissue and pelvic connective tissue must be accepted as of luetic significance, but Nakamura considers them secondary, inflammatory, reactive; Ruge also says he found many luetic endarteritis pictures, while, according to Rieder, they recede almost completely in the background. Nakamura insists he found no real syphilitic vascular changes. In the early stages, however, a cellular perivascular infiltration, panarteritis and panphlebitis are found in the mucosa and submucosa (p. 802) which are plainly gummatous (Orth). Certain cases show distinct gummatous plates in the mucosa and submucosa above the stricture as evidences of their tertiary syphilitic nature. Thus the author saw a 47 year old woman, syphilitic for many years, and repeatedly treated for recurrences, who had, at the upper border of a 32 cm. long constricting ulcer, a number of flat, firm, elevations of gray red color, some round, some lenticular, and smaller. The surfaces of the plaques were slightly depressed or flat and ulcerated. Other ulcers were less elevated, really at the level of the mucosa, suggesting healed typhoid ulcers. Schuchardt and others report similar observations. Bandler who describes the condition as "elephantic and ulcerative changes of the external genitalia and rectum of prostitutes," considers the ulcers of the genitalia which appear before the rectal changes, as parasyphilitic, but amenable to antisyphilitic measures.

The selection of the female rectum is difficult to understand at first, if the changes are syphilitic. But Rieder, Quenu, Hartmann attempt to explain this anatomically by the peculiarities of the rectal veins which anastomose directly with the branches of the external pudendal veins coming to the surface from the posterior commissure of the vulva, while the vaginal plexus communicates directly with the hemorrhoidal plexus. Thus a luetic process of the vulva may reach the rectum by the blood circulation, perhaps helped by the lymphatics. In the male, the virus could reach the hemorrhoidal plexus only by the round about way of the vesical and pudendal plexus. The opinion is steadily gaining ground that it is very often, indeed chiefly a gonorrheal infection (2), a chronic rectal gonorrhea (Wegner, Mucha, lit.; Exner, lit.; Gaucher and LeNoir), which is quite frequent in early stages (according to Huber, 25% of all prostitutes suffering from gonorrhea have gonorrhea of the rectum, but only 1% showed periproctitis). Gonococci invade the deeper layers of the wall which are infiltrated by cells, particularly plasma cells (also present in other chronic inflammatory processes, see Nakamura) and (analogous to a urethral stricture, Huber) they undergo more and more cicatricial change. The abscesses and ulcers, favorable to the development of fistulae are due partly to congestion (Bair) and partly to fecal stasis. But in the rectal gonorrhea of children which is very chronic, ulcers and strictures are rare (Stumpke). In other cases, a gonorrheal inflammation of Bartholin's gland is said to rupture into the periproctal tissue, and initiate these changes.

The preference for the female sex is explained by this etiology, since autoinfection from the genitalia (mechanically by fingers, instruments, vaginal secretion which may be introduced into the anus mechanically) or actual introduction of the organisms by anal coitus (which is rare, Harlose), is much easier in women. According to Jullien, relatively many passive pederasts have rectal gonorrhea. For these reasons a simultaneous rectal-urethral-cervical gonorrhea is frequent, but the rectal involvement may persist, when the cervical and urethral infection has long ceased. It is not remarkable that gonococci from a present (or subsided) uro-genital gonorrhea may reach the rectum through fistulae between vagina and rectum. See Dorsemagen for differentiation by rectoscope between luetic and gonorrheal strictures.

There must also be considered (3): traumata (coitus per anum, enemas with subsequent enema-ulcers), decubitus from fecal impaction, favored in the wide ampulla of the female rectum by constipation and voluntary fecal retention. In these latter cases, the ulcers are often enormous; the author saw the ampulla as big as a child's head with total ulceration of the mucosa, in comparison to which the slight cicatricial periproctitis is quite insignificant. Tuberculosis besides ulcerations may cause cicatricial contraction of the rectum and periproctal tissue. It may be accompanied by replacement of the cylindrical epithelium by squamous epithelium and submucous tissue production, which leads to the formation of papillomata (Sourdille) such as also occur in syphilis. Dysentery must be considered (cf. p. 773, and see Kuenen, Birt and W. Fischer). According to Lewin, leprosy must be remembered. (The case in a 19 year old girl reported on p. 822, shows that clinical mistakes for carcinoma may be made.)

The factors which unify these etiologically different rectal processes, and which make them so similar and differentiation so difficult, are the naturally slight tendency to heal, and the ulcerative disintegration of the mucosa, induced and continued by fecal stagnation (lit. in appendix).

(A rare tumor-like independent cicatricial metamorphosis of the pelvic connective tissue has been supposed to be luetic in origin by Fournier and others; lit. by Herxheimer.)

Tumors of the rectum, see under benign (p. 809) and malignant (pp. 811 and 827), tumors of the intestines.

Intestinal Concretions. Enteroliths

These calculi, formed and increasing in size within the bowel, most frequently in the colon and appendix, which sometimes are embedded in the bowel wall in sacculated recesses, are composed of various substances.

They are concentrically laminated with yellow, white, or brown, stony hard incrustations of fecal masses; they are rarely larger than a chestnut, rounded, cylindrical or bean-shaped; the nucleus consists of a foreign substance, such as ova of ascaris, hair, gall stones, mucus, cellular debris from the mucosa, etc. (p. 834). After outward incrustation, they crystallize inwardly. The layers consist of phosphates, ammonium, magnesium, and organic substances. The brown color is due to bile pigment.

Others are light, porous, semisolid, brown coproliths, a felted mass of undigested plant remnants, mixed with feces, mucus and variable quantities of earthy substances (calcium and magnesium salts), or dry fecal masses desiccated by absorption in the colon (Brosch).

Other calculi are formed from ingested medicinal substances, etc., *e.g.*, magnesia, shellac, salol (H. Leo).

(Abnormally hard fecal masses, composed almost entirely of feces, are called scybala; within, they may be tough and dense, or dry and porous like manure.)

Intestinal Parasites

Merely a summary of the more important intestinal parasites and their pathological significance can be given. Textbooks on zoology contain the details, (*e.g.*, the excellent books of Braun, O. Seifert; see also Marchand, Brumpt, Guiart, Galli-Valerio, Vosgien).

Animal Parasites. Tapeworms, (Cestodes).—Tenia are flat worms without mouth or intestines. The head has organs for attachment (suckers) and is called the scolex. The heads of some tapeworms are armed with a double row of hooklets (rostellum). Lower segments grow by budding from the sexless scolex; through a small neck, the head passes into the proglottides (segments) which bud from the lower, proliferating part of the scolex, and soon develop male and female sex organs (being hermaphrodites). Proglottides are easily detached and may live for some time independently, but finally pass out with the feces. Mature proglottides with attached ova, or embryos (onchospheres, embryo enclosed in an embryonal membrane) then leave their host (are also able to crawl out) and reach the intestinal tract of an intermediary host (change of hosts) in water or food. The membranes are then destroyed and the embryo liberated. These, armed with hooklets, pass through the body wall into the body, or entering the blood stream, are carried into various organs. Then they change (according to type, in 2 to 7 months) into the vesicular, early form of the parasite. If they have found a suitable host, they grow into true tapeworms. This occurs, *e.g.*, with the vesicular echinococcus, the juvenile form of tenia echinococcus in the intestine of the dog, but not in man, in whom it remains as a cyst.

Scolices develop in the larvae, proscolexes of new tapeworms, *i.e.*, new sexless progenitors. If the head anlage is simple, a vesicle develops (cysticercus; see illustration under meninges), which encloses head, scolex (with suckers and hooklets) which may be retracted or projected from the scolex receptaculum. If several proscolixes are developed, a coenurus is formed. The echinococcus develops broad capsules in which the scolices form.

When a vesicle enters the intestinal tract of a new host, further development may take place; the capsule is digested, freeing the scolex. If the host is suitable (as the dog for the echinococcus) the scolex, liberated from the vesicle in the intestinal canal of the new host, may grow into a segmented tapeworm; if the host is unsuitable, only the vesicular, early form is developed.

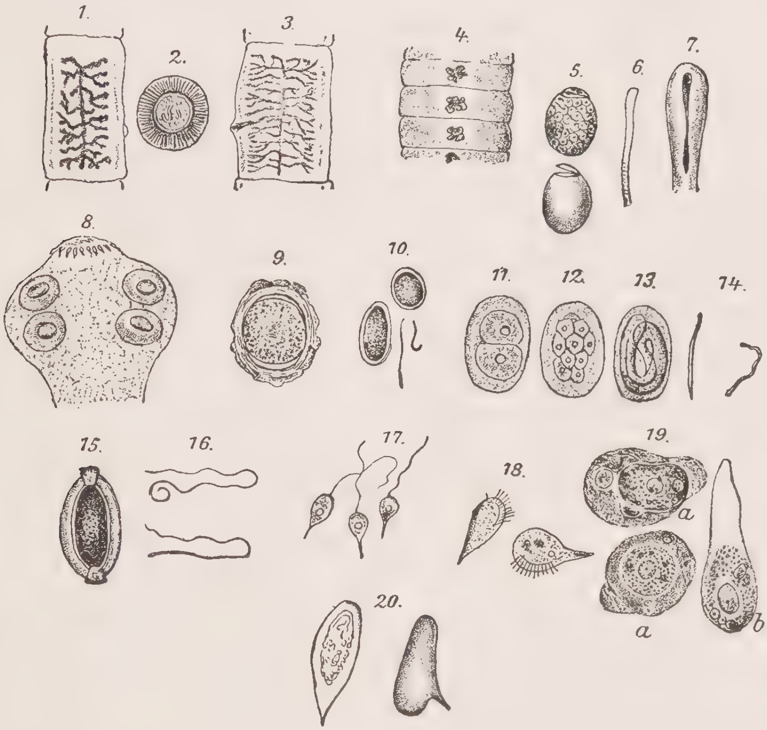
Taenia Solium, or Taenia Armata (Fig. I, p. 849).—This tapeworm, living as a parasite in only the human intestinal tract, is developed from the cysticercus cellulosae of the hog. It inhabits the small bowel, occasionally as multiple individuals. The length is 2 to 3 m., head like a small pin's head, sometimes black, with relatively large, sometimes black, pigmented rostellum, and a ring of twenty-six hooklets, alternating, large and small, recognizable on low magnification, and rather plump in comparison to those of the echinococcus; the four projecting suction cups are lateral. The scolex (head) corresponds exactly to that of the vesical stage (cysticercus). The head is firmly attached to the bowel wall by suction. The neck is about 2.5 cm. long, thread-like, about 900 proglottides.

In the ripe proglottides (beginning about 130 cm. behind the head), the uterus is branched like dendrites. The genital openings are marginal, alternating, situated somewhat behind the centre. There the male and female genital apparatus open; the former is more forward and dorsal, the latter, more distal and ventral. The proglottides are smaller than those of tenia saginata, distally more square, and at last become longer. The duration of its life is estimated at 10 years or more.

Its ova are rounded, with thick, radially striated capsules; diameter about 0.03 mm. The embryo within the ovum is armed with 3 pairs of delicate shiny hooklets (fig. 2, p. 849).

Its larval form is the cysticercus, the true hydatid which is made up of white yellow vesicles, rounded or oval (illustration under muscle), usually of the size of peas to beans, sometimes larger, appearing in man in the brain (*i.e.*, in the meninges, brain substance, or free in the cerebral ventricles) in the intramuscular and subcutaneous tissues, often in large numbers, in the eye (in the conjunctiva, free in the anterior chamber, in the vitreous body or behind the retina), in the heart muscle, more rarely in the lungs and occasionally in the liver, spleen and kidneys, very rarely in the bones; it is said to live from 3 to 6 years, indeed to 20 years. It lies in a smooth walled cyst of connective tissue which is formed from adjacent tissue by irritation. After death of the scolex, the vesicle shrinks and a chalky mass is deposited within. Hooklets remain intact for a long time. The change of hosts occurs in this way: mature proglottides of the tapeworm of man pass out with the feces and are then taken into the stomach of a hog or other mammal (deer, dog, sheep). The eggs and embryos are liberated, the latter pass through gastric and intestinal walls into the organs where they change (in 2 to 3 months) into the vesicular forms (cysticercus cellulosae), a stage passed through by almost all tapeworms. They are ingested as vesicles and embryos into the human digestive tract (relatively frequently by cooks and butchers) with raw or insufficiently cooked, rapidly salted and smoked pork. Sufficient boiling and smoking kills them. The vesicle is digested with the meat, the scolex is freed, locates in the upper small bowel and by segmentation produces its posterior proglottides; in 10 to 12 weeks the segments become sexually mature.

How does the cysticercus develop in human organs? Ingestion of tenia ova-containing embryos is essential. This may occur: (1) by autoinfection as when a host of the tapeworm is careless of defecation, or a lunatic eats his own excrement (external autoinfection), or when the host of taenia vomits and proglottides or ova enter the stomach (internal infection). But simultaneous infestation with taenia solium and cysticercus is very rare; perhaps there is a relative immunity developed by the host of taenia against infection with cysticercus (Henneberg). But the ordinary mode of infestation is from without; *i.e.*, the ingestion of embryo-containing ova into the stomach, in uncooked food, *e.g.*, lettuce fertilized



FIGS. 405–424.—Intestinal parasites. 1. Proglottid of tenia solium (3X). 2. Onchosphere with capsule, so-called ovum of tenia solium (× 250). 3. Proglottid of tenia mediocanellata (3X). 4. Proglottid of bothriocephalus latus (3X). 5. Ova of bothriocephalus latus, the upper contains yolk, the lower empty (× 120). 6. Head of bothr. latus, nat. size. 7. The same magnified (3.5X). 8. Head of tenia solium (× 20). 9. Ovum of ascaris lumbricoides (× 200). 10. Ova of oxyuris vermicularis (× 250); to the left the female, to right the male, nat. size. 11–12–13. Ova of ankylostoma duodenale. Cleavage in various stages (11, 12) and ovum with embryo (× 200). (According to Perroncito and Schulthess.) 14. Ankylostoma duodenale, nat. size, left female, r. male. 15. Ovum of trichocephalus dispar (× 275). 16. Trichocephalus dispar., nat. size. Above male, below female. 17. Cercomonas intestinalis (after Lambl) (× 300). 18. Trichomonas intestinalis. 19. Ameba coli (after Kartulis) (× 730).—aa, the same amebae in various form changes; b, ameba with pseudopod. 20. Ova of distomum hematobium, left with apical thorn, right with lateral thorn (after Leuckart) (× 150).

with human manure. The capsules are digested, the liberated embryos bore through the bowel wall, enter the blood stream, reach the organs and develop into cysticerci.

For the variety called cysticercus racemosus, see under meninges.

Taenia Saginata or Mediocanellata (illust. fig. 3).—(Saginare, to fatten; mediocanellata from the fluted projections of the uterine median canal, visible in alcohol preparations.)

This tapeworm, also living only in man, is the most frequent of these parasites, and occasionally occurs in larger numbers (23, Springer); it develops from the cysticercus of cattle, which is a smaller body (from the size of hemp seeds to peas) than that of the hog. This cysticercus seldom occurs in man (Heller saw it in the eye); it may be mistaken for the cysticercus of the hog without hooklets (see below). Taenia saginata is much longer than taenia solium, from 4 to 8 to 10 m., even up to 36 m. The head has no hooklets, but, according to Kuchenmeister, may show minute points as indications of primary hooklets; according to Heller, embryos, even with numerous hooklets, are not rare. It is somewhat larger than that of taenia solium and more square. The neck segments are macroscopically visible. The segments are thicker and broader than those of taenia solium.

The uterine branching is dichotomous (not dendritic as in taenia solium), the branches are finer, denser, more numerous. The ova resemble those of taenia solium. The cysticerci develop in cattle, usually in small numbers. Infection of man is due to ingestion of raw beef.

In reference to the differential diagnosis between it and taenia solium, it is important to remember that the hooklets may often have fallen out, especially in medicinally expelled specimens of solium (Heller), but mostly, apart from malformation, the dark pockets of the hooklets are still visible. There are also rare degenerated hog-cysticerci cellulosae without hooklets; see Pichler, (lit.).

Bothriocephalus Latus. Pit Head (p. 849, illust. figs. 4, 5, 6, 7).—In its early stages it lives in the muscles and intestines of fishes (pike, salmon, eel); it has no true vesicular stage, but is a solid body (plerocercoid) with a head and tail.

It is not always the longest of the tapeworms (cf. taenia saginata), but may reach a length of 8 to 12 m. with 3000 to 4000 segments, which are broader than long. The head, which is a nodular or lancet, almond or spoon shaped swelling, has two longitudinal suction cups; the neck is long, thread-like; the uterus is situated in the lighter central spot, is rosette-shaped and brown on account of the ova, the lateral areas are yellow. The sexual opening is central on the ventral surface. It may be found as a single specimen, or up to 70 in the same bowel.

Bothriocephalus latus is frequent on the coast of the Baltic Sea, in East Prussia, Pomerania, and especially in the Russian provinces of the Baltic, Japan, Italy, Hamburg, Munich, and the French cantons of Switzerland, but not in central Germany.

The ova have brown capsules, are oval and at one pole have a valve-like operculum; they are 0.07 mm. long and 0.045 mm. wide. The embryos develop in fresh water, free themselves and move with cilia. Its next stage as a plerocercoid is passed in a small cray fish of the plankton, and then, according to M. Braun, in the intestinal wall, body cavity and musculature of fishes (pike, eel, salmon, perch) as larvae (plerocercoids). Tschokke demonstrated this occurrence in the fishes of the lakes of western Switzerland. If the cysticercus enters the human digestive tract (or dog or cat), the bothriocephalus latus may develop, and it is by no means a harmless parasite. Anemia has been observed (Reyher, Schaumann and Tallquist and others), sometimes slight, sometimes severe enough to produce the typical clinical and anatomical picture of progressive pernicious anemia (p. 190). Tallquist extracted a lipoid substance from bothriocephalus latus with hemolytic action in vitro, and he believes this explains the obviously hemolytic bothriocephalus anemia; then Seyderhelm discovered a toxin-like substance in the extract (bothriocephalin) which, by parenteral injection, produced a pernicious anemia in rabbits, not possible with the lipoid substance. The toxin enters the blood from the bowel. It is uncertain whether all bothriocephali are poisonous or whether the toxin is derived from healthy, diseased, or dead parasites. Individual susceptibility of the host must be considered (Schaumann). After expulsion of the tapeworm, the bothriocephalus anemia (p. 190) may be cured or improved, except in advanced cases.

Rare Human Tenias.—Taenia canina or cucumerina is 15 to 30 cm. long, by 2 to 3 mm. broad. Mature proglottides are shaped like cucumber seeds (8 to 10 mm. long, 1.5 to 2 mm. broad). The worm is common in dogs and cats; the cysticercoid stage is passed in the dog flea or dog louse and in the human flea. When these insects, which live in the fur, are crushed by biting and swallowed, the tapeworm develops. Adults and especially small children are infested by contact with dogs and cats. Nervous and intestinal disturbances may develop. Familial infestation has been observed (Lins).

Taenia nana (hymenolepis nana) is 10 to 20 mm. long,.0.5 to 0.7 mm. broad. The rostellum has a simple ring of hooklets; the neck is long, thin as a thread; the proglottides (up to 200) are short and crowded. Eggs are oval, translucent, very numerous. The origin and development are not well understood. It occurs chiefly in children, especially in Italy (Sicily, Crassi and Catandruccio); there are often thousands of parasites in one host. It may burrow into the intestinal mucosa and cause digestive and nervous disturbances. See Schnell in reference to mass infestation with tenia nana.

In reference to other rare taenias, such as taenia lanceolata and taenia diminuta, consult the textbooks of zoology.

Round Worms, Thread Worms, Nematodes (Nemathelminthes).—The trichina spiralis (see under muscles) occupies the intestines temporarily. It enters the bowel as a complete worm in muscle tissue (from pork), while all other round worms enter as ova, to develop into worms.

The Common Round Worm (Ascaris Lumbricoides) (Fig. 9, p. 849).—It resembles an earthworm, pointed anteriorly, male about 25 cm. long; the posterior extremity is bent like a hook and is supplied with two spicules. The females reach 40 cm. in length, the uterus is filled with enormous numbers (many millions) of fairly large ova ($\frac{1}{20}$ mm.) with two capsules, an internal, double constructed, chitinous, and an external, gelatinous, irregularly swollen layer, and are passed with the feces. The embryo-containing ova are very resistant to drying and cold. They are ingested with vegetables, salad, strawberries, etc., or in contaminated water, and develop (in months) into sexually mature male and female worms (feeding experiments by Ebstein). According to recent observations, the larvae of ascarides may wander from the bowel through the liver into the lungs (followed by pneumonia) pass through the capillaries into the alveoli to return through the bronchi, trachea, esophagus into the bowel, an itinerary which requires 6 days in rats and guinea pigs; for human observations, see Steiner. Round worms usually occupy the small bowel in small numbers, but sometimes in colonies of 10 to 20 to 100 (to thousands); they may pass upward by migration or vomiting into the nasal cavity, the larynx and trachea (Furst, lit.), or downward into the colon to be passed with the feces. Round worms contain toxic substances (Flury) and in children, rarely in adults, sometimes cause simple catarrhal to even bloody necrotizing enteritis (verminous enteritis) marked coliky pain, toxic and reflex nervous symptoms. In a 20 year old girl, the author saw bloody fibrinous enteritis and (migration) peritonitis (see Perroncito in reference to helminth toxins). Ascarides may also cause intestinal obstruction (ileus verminosus, very rare, see Miyake, Ruhland) by mechanically occluding the bowel, or by toxic spasm which indeed may involve the entire small intestine (Rost: ascaris ileus). They become of importance by entering and obstructing some duct or by causing pressure atrophy, perhaps with perforation of the bowel (Plew and Spieth, lit. and good illustr.). Active migration very often occurs only after the death of the host; they ascend the duodenum and since they show a predilection for narrow channels, they crawl into a duct (common duct, cystic duct, hepatic and pancreatic ducts); an expelled worm may leave as proof of its former presence a ring-shaped strangulation mark (Ebstein). Living and dead ascarides and ova have been found in ectasias of the common duct (surgical procedure—Fertig, Hinderstoisser, Rosenthal, Horhammer, lit., Kaiser removed operatively 33 ascarides from the bile ducts). They have also been found in the gall bladder (Bremser) and in abscesses of the liver (see there). Sometimes a round worm slips through an intestinal perforation (most frequently of tuberculous ulcers).

Ascaris eggs have been found in the nuclei of fecal calculi (p. 846), and rarely in the center of gall stones.

Ankylostoma Duodenale, Strongylus, or Dochmius Duodenalis, (Figs. 11, 12, 13, 14, p. 849, and fig. 425), a parasite of the intestinal wall.

These small round worms (male 8 to 12 mm.; female 10 to 18 mm., prefer the duodenum and upper jejunum. Their duration of life is estimated at 5 years. They are found in large masses (thousands), rarely isolated, in the intestinal mucosa into which they burrow by means of four claw-like prolongations at the entrance of the bell-shaped mouth capsule which contains in its depths three stiff prongs directed forward. These produce small bleeding ulcers. They feed on the blood and epithelium; perhaps they also suck blood. When they fall off, an ecchymosis remains the size of a lentil around a small triangular hole which may reach to the submucosa. The small wounds continue to bleed (coagulation inhibiting substance (?), see Loeb and Smith). Eosinophilic cells and larger spindle-shaped and rounded phagocytes filled with crystals of various sizes are found in the bowel wall (Cohlein). The loss of blood and diarrhea participate to but slight degree in causing the anemia and weakness in the host (ankylostoma anemia, ankylostomiasis) which is due chiefly to the toxic (according to Ptreti, hemolytic) action of the metabolic products of the ankylostomas (Bert). Such anemias were observed in miners and tunnel workers, as in 20% of the workers who died during the construction of the St. Gotthard tunnel (Sonderegger), the Simplon tunnel (Perroncito);

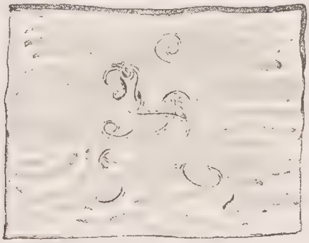


FIG. 425.—Ankylostoma duodenale, several males and females, and trichocephalus with heads attached to mucosa of ileum; found during post mortem of a coolie in Medam (Prov. Delhi, Sumatra); nat. size.

also in German (Menche, Leichtenstern), Belgian (Firket) and Italian brickmakers (brickmaker's anemia) and miners (so-called worm disease or miner's anemia); they cause Egyptian chlorosis, as shown by Griesinger. The eosinophiles of the blood are increased (p. 197). The ova-containing embryos are evacuated in immense quantities into water and there changed into resistant larvae which enter new hosts by the mouth and also, according to Looss (confirmed by many, lit. in appendix) perhaps chiefly, through the external skin, to then develop into sexually mature animals. Penetration of the larvae into the skin occurs both into hair follicles and directly through the epidermis (Schuffner); according to Looss, the route is then as follows: cutaneous veins, the blood into the right heart, lung capillaries, lung alveoli, bronchi, trachea, larynx, esophagus, stomach, bowel. Some enter the cutaneous lymphatics, and then the veins. In the experiments of Looss, the larvae reached the intestines within 24 hours. 7 to 10 weeks after skin infection, the first ova appear in the stools. Ankylostomiasis, endemic in all southern lands, may be imported anywhere and produce severe anemia. In the countries mentioned, it is supposed to be less dangerous on account of adaptation of the inhabitants (Zinn and Jacoby), but this is doubted by others (Wucherer, Lutz, Prowe) and partially admitted by Lohlein from experiences in Camerun where about 82% of the coast negroes have ankylostomiasis (eosinophilia and ova in the feces).

Anguillula (strongyloides) intestinalis, barely 1 mm. long, was found by Normand in the intestines of French soldiers returning from Cochin, China, with severe, sometimes hemorrhagic diarrhea. It also occurs in Japan, America, Italy, etc., and appears sporadically in other places. Leuckart showed that anguillula stercoralis was an externally developed generation of anguillula intestinalis. Its importance is unsettled. Most investigators, as also Leichtenstern, who found the worm in the Rhineland in miners and brickmakers, consider it harmless. But Askanazy found that the worms penetrate the epithelium into the mucosa as far as the muscularis mucosae, absorb chyle and then deposit their ova, which had previously been recognized in this situation by Golgi and Monti, which after changing into embryos, pass into the intestinal cavity. Accordingly, since anguillula intestinalis is a parasite of the intestinal wall, it is probably harmful; see Kurlow who found ulcers, channels and hemorrhages in the bowel wall. The infestation is per skin as in b; see Fulleborn.

Oxyuris Vermicularis, Pin Worm (illustr. fig. 10, p. 849).—The males are 3 to 5, females 10 mm. in length. The posterior end of the male is blunt and somewhat curled, that of the female is pointed like an awl. The latter is cloudy white if it contains many refractile ova, otherwise glassy and transparent like the male and thus difficult to see, especially in the intestinal mucus (Rheindorf). The ova (see illustr. 10, p. 849) are oval and when passed contain an embryo. They are very resistant and remain viable, even after slow desiccation. Oxyuris vermicularis is a very motile little worm and probably the most common intestinal parasite of man (especially in children); its recognition is quite important. It lives (feeding on feces) in the colon and appendix (lit. Schoppler). Colonies are often composed of thousands of individuals and the musoca may be furry from their presence. Conjugation and development of ova take place in the lower ileum. They reach the rectum where the ova are discharged and from which they produce active reflex irritation of the sex organs. They migrate during the night from the anus to the external genitalia and cause itching and reactive scratching, leading to inflammation of the skin, catarrh, erections, onanism, nymphomania. They have been found in the vagina, uterus (Simons), tubes (Tschamer) and even in the peritoneal cavity (see there), especially in Douglas's cul de sac which they reach from the vagina. Oxyuris is transmitted extremely readily through various routes. In most cases, it occurs via the fingers soiled with the ova, or perhaps even entire females under the nails with re-infection of the same individual or new infestation of another, chiefly by food (Heller). Autoinfection may occur again and again, explaining a duration of years in many cases. Complete development of oxyuris takes about 14 days, according to experimental investigation of Leuckart and others (lit. Braun), but five weeks according to Heller.

It is able to burrow into the normal intestinal mucosa (Unterberger, lit.), probably to find food, and it may heal in with the formation of minute calcium nodules (Wagener, lit. Edens). For pseudotuberculosis due to oxyuris or its ova, see under peritoneum, p. 870. In a 31 year old woman, infested for years with oxyuris, the author examined one of the numerous caseous nodules in the colon and mesocolon found at abdominal operation; the oxyuris ova were surrounded by granulation tissue, undergoing fatty degeneration, and broad zone of eosinophiles (lit. Onoufrieff). Appendicitis and oxyuris on p. 833.

Trichocephalus Trichurus (Dispar), Whip Worm (figs. 15, 16, p. 849).—The anterior body is thread-like, as thin as a hair and bent like a whip; the posterior body is thicker, cylindrical and in the male (40 to 50 mm. long, female up to 50 m.) coiled in spiral form. The ova are thick-shelled with button-like bulging at the poles (length 0.05, breadth 0.02 mm.), very resistant to drying, reaching the stomach wind-carried, or with food. It is frequent in the contents of the cecum, appendix and ascending colon as a few individuals (10 to 20) or many. It is spread over the whole world and is apparently a harmless parasite, but it may bore into the upper layers of the mucosa (fig. 425) to suck blood or blood pigment (Askanazy). Children are most frequently affected. Some believe it has pathological importance and causes anemia, intestinal and nervous symptoms, etc. (Stscherbak, Peiper, Schablin, Kappeler).

Flukes, Trematodes.—Family: distoma. The most important are:

(*a*) Distomum hepaticum, fasciola hepatica (large liver fluke). Fully mature, they are about 3 cm. long by 12 mm. wide; the anterior body is fairly thick and conical, the posterior body leaf-shaped. The ova are large (0.13 mm. long) oval operculates with double, strongly refracting shells. It is usually present in the bile ducts and gall bladder, more rarely in the bowel. In the ruminants (cattle, sheep) it may be present in large numbers (hundreds); the liver shrinks from cholangitis, and the animals develop ascites. It is rare in man and only as isolated worms, sometimes with no apparent changes (lit. Blanchod). But coiled together, the parasites may block the bile passages, cause stasis and give the symptoms of biliary cirrhosis of the liver (v. Friedrich); they also produce ulcerations, cicatricial thickenings, incrustations (by bilirubin calcium) and also epithelial proliferations. Eggs may be present by the millions in the gall bladder. If the distomum enters the veins within the liver, it may be carried elsewhere (Leuckart), and abscesses have been found in various part of the body.

Askanazy first described the severe hepatic changes caused by distomum felineum (opisthorchis felineus) on the basis of which even carcinoma has developed (W. Rindfleisch, lit.; more details under bile ducts, p. 1008).

(*b*) **Distomum** (**or Schistosomum**) **Haematobium, Bilharzia Hematobia** (fig. 20, p. 849).—Bilharzia has long been endemic in Egypt. Ruffier found calcified ova in the kidneys of mummies of the XX dynasty (1250–1000 B.C.). It was discovered by Bilharz in Cairo in 1852, where it is frequent in the poorly nourished, especially, although not exclusively, young males (Fergusson); it occurs also in Abyssinia the African east coast, Tunis, etc.

There are separate sexes; the body of the male is rolled like a drain pipe (gynephorous canal) to retain the female which is thin and long. The parasite lives, paired, in the abdominal veins, portal vein (may cause cirrhosis of the liver) and its branches, and especially in the veins of the pelvis where it feeds on blood. Its ova which have a hook or point (size 12 to 19 by 5 to 7 microns) are deposited in the smaller veins of the mucosa and submucosa of the renal pelvis, ureters, especially the urinary bladder, colon, the rectum, and the genitalia. Alterations in the bowel consist first of hyperplasia, then atrophy of the mucosa with erosions, some with the formation of polyps (ova in the feces). Catarrhs develop in the urinary tract with marked swelling, and suppurative, often diphtheritic, inflammations (Dopter, lit.), hemorrhages and incrustations, but rarely calculi (Pfister) with ova as the nuclei, ascending renal inflammation; blood and fat, molecularly divided, then appear in the urine (hematuria and chyluria). The thickened mucosa of the bladder may develop benign polyps in which numerous ova may be imbedded or carcinomas (irritative carcinoma). Ova are found in the urine (lit. Goebel). Consequences are anemia (eosinophilia of blood), marasmus, amyloidosis. Transmission is through contaminated water, by drinking and bathing, probably also via the urine. Passage through skin is probable (lit. Looss and Kartulis).

Schistosomum Japonicum (Tsuchiya, Katsurada and others) resembles Bilharzia, but, among other differences, it has much smaller eggs and is without thorns. The paired parasites inhabit chiefly the portal vein and its mesenteric branches (urinary bladder remains free). Consequences: chronic catarrh of the colon, with ulcerative changes, bloody stools, swelling of the liver (cirrhosis of liver), splenomegaly, anemia and fatal cachexia (the Katayama disease of Japan and China). On the basis of these chronic inflammations, atypical proliferations and also carcinoma of the bowel may develop. Ova may be carried into the internal organs, such as the liver (eventual cirrhosis), mesenteric lymph nodes, and even into the brain (softening, irritation, epilepsy). They enter the skin from water (laborers in rice fields) (Nakamura, Tsuchiya and Katsurada).

Distomum lanceolatum (dicrocoelium lanceolatum), lancet-shaped 8 to 10 mm. long, 1.5 to 2.5 mm. wide, is very rare in man; it is often present in herbivorous and omnivorous mammals, in company with distomum hepaticum.

For distomum pulmonale, see under lung, p. 481.

Protozoa.—Details by Ad. Schmidt and J. Strasburger, Die Fazes des Menshen, III Edit., Berlin, 1910, (lit.), and Roos, "Die im menschlichen Darm vorkommenden Protozoen and ihre Bedeutung," M. Kl, 1905, 52 (lit.). Also: Doflein, Lehrb. der Protozoenkunde, Jena, 1911; Hartmann a. Schilling, Die pathog. Protozoen, Berlin, 1917, a. Schilling in Lehrb. d. Mikrobiologie von Friedberger-Pfeiffer, 2Bd, 1919.

The Rhizopoda, Flagellata, Infusoria and Sporozoa

Rhizopoda.—Ameba coli and entameba histolytica, the ameba of dysentery, are rhizopods (p. 772). Entameba buccalis found in dental tartar and in carious teeth is not pathogenic (W. Fischer).

Flagellata.—Trichomonas intestinalis (Leuckart), pear-shaped body with four flagellae, 0.01–0.05 cm. long, is found in acute and chronic diarrheas, occasionally in the feces in typhoid fever and cholera, but also in the healthy. Grassi identifies this with the cercomonas intestinalis (illustr. 17, p. 849), but Janowski separates them. Trichomona intestinalis is quite certainly identical with trichomonas vaginalis (Donne) which lives in the vagina and intestine and also occasionally in various other organs, externally accessible (mouth, stomach, lung, urethra). Lamblia intestinalis (megastoma int.) is found in normal stools in an encysted condition (oval cyst, 13 to 8 cm. in diameter, 2 nuclei and an arched flagellum). Its vegetative form (pear-shaped, an excavation at anterior end, 4 pairs of flagellae) has been found in intestinal catarrhs (which it perhaps causes), also in the feces in typhoid fever and cholera, and in the stomach (in carcinoma). Located in the small bowel, it also occurs in rats and mice.

Sporozoa (such as coccidia, hemo- and sarcoporidia) will not be discussed, but coccidia have been mistaken for oxyuris ova (Hueter).

Infusoria have flagellae with which they move, and cilia.

Balantidium coli (from the intestinal tract of the hog) may cause inflammations and ulcerations, especially in the colon, by penetrating the intestinal wall (lit. by Dopter, Lohlein, Behrenroth, lit., Schoppler, Jaffe).

Vegetable Parasites (see p. 857).—While the meconium (pp. 360, 719 and histology by J. E. Schmidt) is sterile directly after birth, in a few hours various microorganisms can be demonstrated in the newborn intestinal tract (entrance by mouth and anus; Escherick). Later, bacteria are present in large numbers, such as colon bacilli, bac. aerogenes capsulatus which is identical with bacillus phlegmones emphysematosae, and the immobile, strictly anaerobic butyric acid bacillus of Schattenfroh-Grasberger (Passini, Pommer and others), staphylococci, streptococci, including streptococcus lacticus (v. Wiesner), diplococci, proteus forms and others; these are generally harmless saphophytes. The organism present in greatest number, called bacillus coli commune, may become important; it resembles the typhoid bacillus and can be differentiated only by special methods. The contradictory statements in reference to bacillus coli communis make it obvious that it is not a uniform kind of bacteria. Bacterium coli is found in varied circumstances, thus in gangrenous hernias, in which it passes through the bowel wall, in inflammatory processes, especially of the abdominal organs, such as perforative peritonitis, purulent peritonitis without perforation, suppuration of bile ducts, the liver, kidneys, the bladder, even in metastatic meningitis originating from abscesses of the liver, uterine diseases, etc. (Intestinal bacteria and bacillus coli by Kruse.)

THE PERITONEUM

The peritoneum is a fibrous membrane containing numerous elastic strands covered by a single layer of cells, and traversed by blood and lymph vessels. The peritoneal cavity, like other serous cavities, is an adnexa of the lymph tracts (Klemensiewicz) not a true lymph space (Weidenreich), from which it differs by its cell lining, contents and function (Marchand). Its absorptive power is very great; diffusion into the blood takes place readily but more readily into the lymphatics, between the loosely connected lining cells (McCallum, lit.); formerly, it was believed that absorption took place through stomata (v. Recklinghausen) or open communications between the lymph vessels and the peritoneal cavity. The central tendon of the diaphragm is especially fitted for absorption, but the process also occurs in the omentum and other parts of the abdominal serosa which drain into the thoracic duct (Arbeiter). Fluids, gases, and even particulate elements, such as pigment, bacteria, etc., may be quickly absorbed and carried to the mediastinal lymph nodes and the thoracic duct. In experimental poisoning (*e.g.*, sublimate) and after the introduction of bacteria, it is seen that the absorptive power of the peritoneum is so great as to be almost equivalent to intravenous injection (Muscatello, and see lit. in appendix to p. 865, in reference to peritoneal absorption). Lymph tracts pass through the diaphragm into the pleural sac (and vice versa), as Kuttner demonstrated by injection preparations.

In reference to the functions of the omentum, see Seifert; for the marked phagocytic properties of the histiogenic wandering cells, derived from the so-called milk spots of the omentum, where they are present as pyrrhol cells, *i.e.*, in vital staining with pyrrhol-blue, the pigment is stored in their granules, see J. Koch, lit. by Marchand, and Aschoff.

Non-inflammatory Changes of the Contents of the Peritoneal Cavity

Ascites, Hydrops of the Peritoneal Cavity.—A fluid transudate collects in the abdominal cavity, sometimes 10 to 20 and more litres, water clear or amber in color.

This fluid is diluted, watery blood serum; it contains much less albumen than blood serum, usually about 2.5%, but in cirrhosis of the liver 4 to 4.5%, and its specific gravity is less (1.004 to 1.014). It contains but few, or no loose fibrin coagula.

Cells are sparse; microscopically, some desquamated, fatty or disintegrating lining cells, some leucocytes, swollen or containing fat granules can be found. After death, more lining cells are detached from the serosa and the fluid becomes slightly cloudy. Fatty degeneration of many cells causes opalescence.

Ascites is analogous to (free) hydrops of other serous cavities, such as the pericardium and pleural sac and to edema (infiltrated hydrops) of the subcutaneous tissues (anasarca) all of which frequently appear together.

If the quantity of fluid is large enough it forces the diaphragm upward and impedes respiration; in marked ascites, the posture of the body resembles that of a pregnant woman. The epigastric veins (sup. and inf.) are prominent in the abdominal walls; the umbilicus may be flat or even protruding; diastasis of the tissue of the abdominal wall may occur as in pregnancy (striae, linea alba).

Ascites is due to the following causes:

(*a*) Venous congestion, most often from disturbances of the portal circulation (cirrhosis of the liver) and cardiac and respiratory (emphysema) diseases.

(*b*) Cachexia in chronic diseases with impoverished blood, anemia, or great loss of body fluids, such as chlorosis, syphilis, carcinoma, chronic profuse suppuration, and especially chronic kidney diseases.

For general remarks in reference to hydrops, see p. 2.

(*c*) Local diseases of the peritoneum, *e.g.*, tuberculosis, primary and secondary tumor, *e.g.*, surface papillomata of the ovaries, but, in such cases, the ascitic fluid is often serohemorrhagic and wine red. The dividing line between transudate and exudate is often abolished. While in the cases mentioned, ascites is a secondary affliction, in young girls before puberty an idiopathic ascites occurs due to a subacute serous peritonitis which disappears in some weeks, or after the first menstruation (Quincke).

Special Forms of Ascites.—Chylous ascites is due to lymph pouring into the peritoneal cavity, caused, among other things, by rupture of a branch of the thoracic duct, as in carcinoma of the duct (Heydecker), or the rare rupture of a mesenteric lymph vessel (see under lymph vessels); the fluid is milky and opalescent like chyle (Bargebuhr, Pagenstecher, lit., Loffler, lit.). In adipose ascites the transudate does not coagulate, even in days, but contains fat, microscopic fat granules and molecular fat. Tumor cells undergoing fatty degeneration may also cause cloudy ascitic fluid. Admixture of blood causes it to be red, often bright red; in icterus the pigments stain it dark yellow to green.

If the ascites occupies closed spaces formed by peritoneal adhesions, it is called ascites, or hydrops saccatus.

Changes in the peritoneum from long continued ascites consist of insidious chronic inflammations. The cell layer is thickened and the membrane is cloudy and white. After fatty degeneration has developed some of the cells are exfoliated (epithelial catarrh). But cellular infiltrations and proliferations of peritoneal connective tissue also produce flat, white thickenings, or small thread-like, granular or villous connective tissue proliferations which on account of venous hyperemia may be gray, bluish red or slate-gray. Such proliferations frequently lead to adhesions.

Free Hemorrhage into the Abdominal Cavity (Hemoperitoneum).—Intra-abdominal hemorrhage, blood in the abdominal cavity, is found after faulty hemostasis in operations, trauma (fall, blunt force); branches of the superior mesenteric artery, or the spleen, or most frequently the liver may be torn.

The author saw rupture of the spleen due to crushing by a railroad car in a robust conductor with several fractured ribs on the left side; he lived 20 hours; condition not bad at first, then he showed symptoms of internal hemorrhage; 1800 cc. fluid blood were found in the abdominal cavity; the splenic surface showed a deep T-shaped tear.

Other causes: spontaneous, often massive hemorrhages, fatal in a few hours (more than 2.5 litres, an average 1800–1900 cc. are sufficient to cause death) may come from a ruptured tubal gestation (see there) or from an ovary (Graafian follicle, corpus luteum; previous ovarian gestation with completely expelled ovum).

Forssner admits only the latter possibility, but Barolin recognizes the follicles and corpora lutea as sources of larger hemorrhages, and in four observations he could exclude gestation histologically (the only deciding investigation) (see Urban).

Tumors and tuberculosis with new, easily torn vessels, ruptures of aneurysms (especially of the aorta), may cause considerable hemorrhage.

Occasionally, the amount of blood in the peritoneal cavity is small in spite of severe injury to the liver. In a 23 year old soldier of herculean development who was crushed by a cave-in, the author found four deep, gaping tears across the liver, parallel to each other; anteriorly in the right side of the right lobe there was an area of destruction larger than a fist; it was discolored, necrotic, hemorrhagic and bile stained; numerous thrombosed vessels were seen, but there was only 100 cc. of fluid blood in the abdomen.

Rarely, an angioma or other tumor of the liver is ruptured. In a woman 40 years old, the author found 2700 cc. pure blood in the abdominal cavity which came from a ruptured, vascular, soft carcinoma nodule on the liver surface with primary carcinoma of the pylorus. (Other cases, see p. 967, secondary carcinoma of liver.) For life-endangering intra-abdominal hemorrhages from or with uterine myomas, see Weber, Benzel, lit. Schnyder saw fatal hemorrhage from the gall badder (consult under gall bladder); see Maas in reference to rare abdominal hemorrhages.

Fate of the Escaped Blood.—Blood poured into an intact peritoneal cavity (capable of absorption) is partly, or if it is quite fluid, completely absorbed. Coagulated masses sometimes remain longer in the deeper places (especially in the pelvis) and by local irritation cause tissue production, whereupon they are gradually absorbed or encapsulated (see retro-uterine hematocele). Part of the blood pigment may remain permanently and become black or brown from the action of sulphuretted hydrogen from the bowel (iron sulphate); occasionally the peritoneum over large areas is covered with minute dots of pigment (like snuff). The remains of old extravasations may undergo fatty degeneration and calcify.

Circulatory Disturbances

After sudden relief of abdominal pressure, such as after removal of ascites or excision of a large tumor, an active congestive hyperemia occurs, causing active injection of the finest vascular twigs of the serosa, similar to a fresh inflammatory process. Hemorrhages in the peritoneal membrane may take the form of small petechiae, or if the subperitoneal tissues are also saturated, large hematomas.

Hemorrhages occur in the hemorrhagic diatheses, subsequent to congestion, spontaneous rupture of altered, sometimes aneurysmal vessels, etc. In the kidney and pancreas regions, quite considerable, sometimes fatal, hemorrhages are not infrequently due to spontaneous rupture of vessels (see pancreatic apoplexy). When aneurysms of the abdominal aorta rupture (p. 143), the peritoneum is lifted upward by hematomas larger than a child's head which finally rupture.

A smooth pseudomembranous capsule may form, exactly like a serosa, around intraperitoneal hemorrhages (consult retrouterine hematocele under female genital organs). Repeated hemorrhages, as in gynatresias, may lead to numerous peritoneal adhesions.

Inflammations of the Peritoneum. Peritonitis

Differentiation is made between acute and chronic peritonitis:

Various forms of exudative and productive inflammations are met, the histological details of which have been discussed in part under other serous membranes, such as the pericardium, pleura. Of special interest are the numerous mononuclear cells (monocytes, p. 196) in the exudate, frequently appearing as macrophages; as to their source, histogenic, especially from wandering cells of the omentum, many opinions are expressed (Marchand, lit.). The lymph spaces around the nerve plexuses of the intestinal wall (p. 718) sometimes contain granular, thready masses of exudate in acute peritonitis, (Askanazy), but, according to Walbaum, this is not the rule; their presence may possibly explain the occurrence of intestinal paralyses.

Acute Peritonitis. This originates from some organ of the abdominal cavity or as a reaction to bacteria introduced from without, *e.g.*, during operative procedures. An hematogenous origin is rare (starting from angina, etc.); according to its extent, it is diffuse or circumscribed.

The term, central peritonitis, is used if it occurs between the loops of small bowel, and peripheral if it occupies the periphery of the pelvic cavity, upper abdominal regions, sides, pelvis, etc. According to the extent of the exudate, Enderlen differentiates (*a*) circumscribed, (*b*) free, (*c*) diffuse, in which (*b*) is the connecting link.

The picture of fully developed, violent, general peritonitis is very characteristic. At autopsy, the abdomen is much distended and the percussion note is tympanitic. On opening the abdomen, the loops of intestine escape, and may easily be cut unless due care is exercised. The intestinal loops, much distended during life by gases (meteorism), due to the loss of contractility (intestinal paralysis) are markedly injected, reddened, sometimes filled with numerous petechiae (vascular paralysis), covered by gray, gray yellow or yellow red exudate, recognized by scraping with the knife (completely absent in extremely acute cases). They are cloudy and fatty and feel slippery and soapy. There are often red stripes extending along the loops, well demonstrated by pulling apart adherent loops. This arrangement corresponds to regions between the loops which are three cornered spaces on cross section; these spaces may be viewed as a system of communicating tubes in which there is hyperemia, and as the place of least resistance, where the exudate is absorbed (Wilks and Moxon). The adjoining portions of loops become adherent, thus often localizing and confining the exudate. The serosa is edematous; on separation it tears easily and may be pulled from the muscularis, proof that the layers are saturated with fluid. Thus, peritonitis attacks the bowel from without. According to Enderlen and Hotz, the subsequent intestinal paralysis is not due to this parietal infiltration, but is secondary to stasis of the contents, which is caused by suspension of absorption and hypersecretion; this disturbance of activity is perhaps brought about by vasomotor disturbances from the general infection.

Causes.—The inflammation is caused by (*a*) chemically active substances (stomach contents, bile, blood, cyst fluid, transudates in certain cases of nephritis, etc.). In this so-called chemical peritonitis, it must be remembered that bacteria may be overlooked if examinations for anaerobic forms are not made (Hyde); (*b*) by bacteria (and their toxins) most frequently streptococci, staphylococci, colon bacilli (Malvoz) and also obligate anaerobes (Ghon, Runeberg, lit.); pneumococci are frequent, usually in fibropurulent exudates and in some cases with a tendency to encapsulation (abscess by fibrin, *i.e.*, organization, lit. by Jensen, v. Brunn, Ghon, Koeneke, lit.); more rarely, the organisms are influenza or typhoid bacilli or gonococci, when the peritonitis is frequently fibrinous and diffuse or more circumscribed and relatively benign in its course. The latter are often present with other organisms. Indeed, several kinds are found in most cases of peritonitis due to perforation, and according to Friedrich, anaerobes are the most important of all. In hematogenous peritonitis one kind is present, as a rule. Tissue lesions or fluid contents (blood, ascites) in the abdominal cavity supply a point of attack and a good culture medium for bacteria, and the fluids also favor extensive spread. From the freshly infected peritoneum, bacteria promptly reach the blood by absorption into the lymph vessels (Fromme and Frei, lit.).

The exudate is derived from the blood vessels and varies corresponding to the various forms of origin; it is chiefly fibrinous at the beginning or permanently (with thread-like, spider web-like or furry arrangements), and thus dry, or is fluid when it is abundant and may be serous, cloudy-serous, or sanguino-serous, sero-fibrinous, fibrino-purulent, purely purulent, purulent-suppurative. Various forms of exudate are often seen in one case.

The condition of the peritoneum in general peritonitis is seldom uniform. If one imagines, *e.g.*, a septic disease of the uterus (puerperal fever) as the cause, creamy pus may be found in the pelvis on the sides of the abdomen and between the loops of the ileum, while on them, and in the upper abdomen, there is merely intensive reddening and spider web-like exudate.

Sero-sanguinous exudate, without fetor in puerperal infections is characteristic of bacillus phlegmones emphysematosae (Eug. Fraenkel; Bingold).

Bile peritonitis may develop from injuries or spontaneous perforation of the gall bladder and escape of infected bile. (The author saw the condition in rupture of small superficial vesicle-like bile ducts with cholangitis; Ermer, lit.) There has also been observed a bile peritonitis of serous or purulent character, markedly bile stained, without perforation of the gall bladder; this is due to percolation and filtration of bile through the wall (Clairmont and v. Haberer), *i.e.*, a form of diapedesis (Konig) by diffusion through diseased walls (Schoemaker), or after digestion of the gall bladder wall by pancreatic trypsin (Axel, Blad), or from minute tears or microscopic gaps in continuity (Nauwerck, Sick and Eug. Fraenkel, Louros, lit.). (Lit. by Posselt, Fibich, comp. Neuber.) Escape of pure sterile bile has been called bile leakage, or cholascus (Landau) to differentiate it from bile peritonitis; but here also fibrinous and serofibrinous peritonitis is occasionally observed (Heilmann, Louros, lit.). Bile itself is an irritant and causes inflammation. It is of clinical interest that the pulse rate may fall to 48, possibly due to absorption of bile components (Finsterer).

The form and extent depend on the origin and inflammatory factors, *i.e.*, the causes of peritonitis, and accordingly differentiation is made between primary and secondary peritonitis.

Primary Peritonitis.—Organisms may enter the abdominal cavity directly through perforating trauma or operative procedures. Even without opening the abdominal cavity, blunt forces may injure the abdominal organs sufficiently to cause escape of their contents. The more severe the tissue destruction and the hemorrhage accompanying the trauma, the more favorable are conditions for the organisms and the earlier the development of the peritonitis.

Contusions to the abdomen occasionally cause peritonitis without demonstrable lesions in organs containing bacteria, *i.e.*, especially the intestines. Whether this is a migratory or hematogenous peritonitis, *e.g.*, from an angina accidentally present, is often difficult to decide (Weichsel). Peritonitis does not always develop when bacteria enter the peritoneal cavity. Its great powers of absorption, the prompt phagocytosis by leucocytes, etc., the bactericidal power of the peritoneal fluid, according to Schiefferdecker (D. 25, 1906, lit.) probably of the omentum too, as experimentally demonstrated (Grawitz and others) may allow fairly large quantities of (not highly virulent) pyogenic organisms to be introduced into the abdomen of animals without consequences. In reference to peritoneal absorption, which, according to J. Koch, is almost exclusively through the great omentum and the central tendon of the diaphragm, see p. 858, and lit. in appendix. But if tissue lesions, however slight, or if chemical irritants are present, conditions are created which favor the growth of bacteria. But virulent bacteria in large numbers (plus toxins) are direct causes of peritonitis (Clairmont and v. Haberer), as are the toxins alone of killed cultures which by chemical action may produce suppuration (Grawitz); large quantities of toxins kill the animal. Similar cases in man lead to general infection in a short time, and are called peritoneal sepsis; at autopsy the local peritoneal signs (septic peritonitis) are relatively mild, but bacteria are found in the blood and organs. According to Lennander, a greater danger than direct peritoneal infection lies in absorption of toxins from the intestine paralyzed by infection, and in the migration of intestinal bacteria.

Secondary peritonitis, circumscribed or diffuse, is much more frequent and accompanies other pathological processes. By bacterial migration, by extension, by continuity, from perforation of an organ or focus, or by metastatic transmission of organisms, a peritonitis develops. Accordingly, it is differentiated into: migratory, continuity, perforative and metastatic peritonitis.

The diseased organs leading to migration, continuation or perforation are:

1. Organs in the peritoneal cavity, *i.e.*, (*a*) stomach, duodenum, other parts of the intestines. Peritonitis is due most frequently (especially in children) to appendicitis (p. 837), in which, according to Runeberg, obligate anaerobes with powerful toxins are the chief offenders. Migration

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of bacteria (chiefly pneumococci, Rohr, lit.), is frequent without perforation, especially in the intestines; migration is favored by circulatory disturbances, stagnation, slight lesions of the mucosa, even catarrhal changes (p. 759). (In reference to the many other ulcerative and necrotic intestinal processes, see under respective headings); (*b*) liver and bile ducts, especially from ulcerative calculous disease; (*c*) spleen (see perisplenitis, p. 245); (*d*) lymph nodes, which may become necrotic as in typhoid fever (p. 794) or undergo tuberculous softening and rupture (Iselin); (*e*) the intra-abdominal and subserous fatty tissue, which, as discussed under pancreas, undergoes a peculiar fat necrosis and occasionally produces peritonitis (rare); (*f*) tubes, uterus and ovaries, the two latter especially in puerperal processes, produce a diffuse peritonitis or circumscribed pelvic peritonitis.

2. Organs lying extraperitoneally, such as pancreas, kidneys, male genitalia, female genitalia (in part), as in a subperitoneal suppuration in the parametrium (parametritis) which extends to the peritoneum by continuity, and leads to a pelvic or a general peritonitis. By continuity, a peritonitis may be due to infected retroperitoneal lymph nodes and caries of bones, especially of the vertebrae. Peritonitis is rare in diseases of the bladder without perforation (lit. by Retzlaff). The author repeatedly saw peritonitis follow retroperitoneal phlegmons in pelvic bullet wounds.

Cases in which an inflammation of a retroperitoneal organ is followed by a more extensive inflammation of retroperitoneal cellular tissue might be called retroperitonitis (Babes).

3. Inflammations of the lung, pleura, pericardium by continuity are often communicated to the peritoneum through the diaphragm. The reverse also occurs. The route is via the lymphatics (Kuttner); some think that the bacteria must "grow" through the diaphragm (Ernst Burckhardt, lit.). Usually the inflammation is localized to the vicinity of the splenic and liver surfaces. A periesophageal and a peritracheobronchial phlegmon may continue along the stomach to the peritoneum, as after the use of the bougie in strictures or following attempts to extract foreign bodies from the bronchi.

4. Peritonitis may also be secondary to inflammatory changes in the abdominal walls, *e.g.*, phlegmons subsequent to wounds, etc.

In purulent peritonitis, the direction taken by the inflammation may be opposite to that usually traveled, *e.g.*, from the serosa of the appendix to the muscularis (Sugi).

Generally speaking, perforative peritonitis is more dangerous than peritonitis due to continuity, because, as a rule, both bacteria and irritant chemicals, such as intestinal contents, chyme, bile, urine, are poured into the abdominal cavity, the fluid of which spreads promptly over a larger area. Perforative peritonitis is fatal in most cases, the more contents that escape, the more quickly death results. The worst changes in the peritoneum are observed in peritonitis due to continuity, as a rule, at the starting point, and in its immediate vicinity. The exudate usually sinks, in the recumbent position to the deepest parts of the abdomen, the pelvis and in the lateral spaces.

If gas also enters the peritoneal cavity (pneumascos) (Ponfick), it collects in the upper abdomen, especially between the liver and the diaphragm; at autopsy, this part may be remarkably dry and the surface of the liver rounded, or flattened, or concave, or bowl-shaped, from the pressure of the gas. Occasionally, the formation of gas in the free abdominal cavity causes enormous distension of the abdomen (Falkenburg, Frund). On opening the abdomen the air escapes with a hissing sound. Tension pneumascos in perforated gastric ulcers and valve-like action of the opening which permits air to escape, but not to reenter the stomach, are described by Brunzel.

Sometimes in perforative peritonitis, but more frequently in peritonitis due to continuity, encapsulation of the exudate occurs, *e.g.*, in the subphrenic spaces from ulcerative processes in the stomach and duodenum; adhesions in the neighborhood, or adjacent viscera, or especially the omentum, or parts of organs (liver, stomach, uterus, etc.), surround the focus of inflammation as a protection and confine the exudate. Sometimes even a channel or conduit may be formed.

Thus, *e.g.*, exudate from the uterine adnexa may be conducted alongside a loop of lower ileum into the cecal region and from here along the outside of the ascending colon to the right hypochondrium, along the lesser curvature of the stomach to the cardia where it collects, and except in the pelvis, there is no other focus of exudate and hardly a trace of peritonitis. The process is an example of a "peripheral" peritonitis.

Sometimes favorable grouping of adjacent organs surrounds the exudate permanently until by gradual organization, it is solidly encapsulated; this occurs most frequently in the appendiceal region (p. 837) and in the pelvis (diseases of the adnexa). It is spoken of as "intraperitoneal abscess" or "abdominal empyema" (Lennander; comp. "subphrenic abscess," p. 838). The encapsulated focus may be uni- or multilocular with a communicating system of cavities, the contents of which vary; following a perforative appendicitis (boy 8 years old), the cavities contained white, cheesy, creamy and light green contents.

The escape of intestinal contents causes stercoral peritonitis, and if rupture occurred into a walled off space, or adhesions were promptly produced, there is a local suppurative purulent inflammation, the so-called fecal abscess.

Hematogenous or metastatic diffuse peritonitis of purulent character is sometimes observed in puerperal fever, pyemia, injuries of distant parts, in typhoid fever, and other infectious diseases (articular rheumatism, scarlet fever, diphtheria) and possibly in tonsillar angina (de la Chapelle, lit.). These forms are relatively rare.

So-called cachectic peritonitis is particulatly prone to occur in late stages of chronic nephritis (probably from the chemical irritation of the peculiar transudate), cardiac diseases, leucemia, etc. The exudate is serous, fibrinous or purulent.

Idiopathic peritonitis sometimes occurs in the syphilitic newborn. Other cases of peritonitis are sometimes seen, even in the fetus, although rarely.

Chronic Peritonitis. Chronic peritonitis, with the tendency to produce connective tissue, is sometimes seen as the conclusion of an exudative inflammation (healing); it also appears insidiously and is chronic from the beginning as in cirrhosis of the liver, large ovarian tumors, etc. According to its extent, it is spoken of as local, the usual type and general, chronic peritonitis. A dry and a moist form may be differentiated. The latter is sero-fibrinous, not rarely hemorrhagic, and sometimes purulent. A chronic fibrinous peritonitis leads to numerous adhesions from the organization of the exudate (chronic adhesive peritonitis); the abdominal viscera may be fused to an inseparable mass with each other and with the parietal peritoneum (deforming peritonitis). It may be almost impossible to open the abdomen at autopsy without continually cutting into the bowel. In such cases, remove first the abdominal skin, try to enter the abdominal wall laterally, separate it from the bowels in the lower and upper abdominal regions. If this is impossible, it is advisable to first open the thoracic cavity and remove the heart and lungs, then the organs of the neck, aorta and esophagus as a whole, then all the abdominal and pelvic organs as a whole, after separation of the diaphragm. The autopsy is thus made from behind. Begin with the spleen, kidneys and large vessels, and progress slowly. The intestinal loops tear easily in any attempt to separate them, which is best done under water.

See Marchand in reference to the relation of the lining cells to the formation of connective tissue and consult his literature.

In purulent peritonitis of some duration (weeks, months), the loops of the small bowel become fused into an unrecognizable convolution and lie firm and flat against the spinal column. The omentum is thickened and lies rolled up between the transverse colon and stomach or in front of the colon. In rare cases, ulceration occurs in the infiltrated areas (ulcerative peritonitis) which may lead to abscesses outside of the peritoneal membrane. Purulent peritonitis may also lead to perforation through weakened areas of the abdominal wall (inguinal region or around the umbilicus) or into the viscera, especially the bowel.

There are also cases of chronic peritonitis in which there is general thickening of the peritoneum without adhesions. The omentum and mesentery become tendonous, white, hard, and contract considerably (scirrhus, contracting, chronic fibrous peritonitis). A rare form of chronic sclerotic and contracting peritonitis may occur over the liver (see there) and spleen, occasionally throughout the entire peritoneum, especially over the intestines and stomach (see there) with retraction of these organs by cicatricial infiltration of their walls, and "zuckerguss" thickenings of the non-fused layers of the pericardium. Nicholls (lit.) calls this "progressive hyaloserositis" (lit. by Huguenin), Gofferje (lit.), "fibrous polyserositis." This chronic, fibrous, hyperplastic polyserositis, usually accompanied by ascites, is of much practical importance, because of its resemblance to diffuse carcinoma; it is called by the French "liente plastique" (lit. by Curtis, Esau). The author has seen cases mistaken clinically for cirrhosis of the liver. The etiology is obscure; the chief factor may be chronic venous congestion, or an infectious process from various organisms (Neusser); according to Wiexkowski, it is toxic, chiefly from endotoxins of tubercle bacilli. These latter opinions are still to be proved (v. Mahrenholtz; see under stomach, p. 668).

Local chronic fibrous peritonitis is much more frequent than the general form. It is observed in the hepatic region in syphilis, tuberculosis, cirrhosis of the liver, gall stones, in the splenic region (see perisplenitis, p. 245), in the female pelvis (irritations following puerperium, abortion, endometritis, salpingitis, especially gonorrheal, etc.) when it produces displacements of the uterus, kinking of the tubes, sterility, extrauterine gestation, etc. Corded or spider web-like adhesions of the pelvic organs are present in practically every prostitute. They are also found in the gastric region (round ulcers), the ileum, the ileocecal region and in the vicinity of the appendix (with all sorts of inflammatory processes), the sigmoid flexure with adhesions and volvulus (p. 748 and fig. 355, p. 752), in hernias, in the neighborhood of mesenteric lymph nodes, around tumors (especially carcinomas), etc.

A chronic fibroplastic omentitis glues the parts of the omentum to each other and to other parts of the peritoneum.

The dangers arising from peritonitic bands were pointed out on p. 748 under internal incarceration of the intestine.

Retraction of peritonitic granulation tissue may narrow the lumen of the bowel, or in acute peritonitis, an intestinal loop is compressed by superimposed adherent loops, or adhesions and fixation will kink a loop at an acute angle.

The formation of numerous sand grains is very rare; they may be calcified, concentrically layered endothelial cells of lymph vessels which have undergone hyalin degeneration during a chronic peritonitis (peritonitis arenosa, Virchow). Borst calls them "psammomas." See p. 875 for gland-like proliferations of lining cells.

Infectious Granulation Tumors

Tuberculosis.—This is very frequent and must be differentiated into simple tuberculosis and tuberculous peritonitis.

Etiology.—Tuberculosis is often secondary to intestinal ulcers, caseous lymph nodes, tuberculosis of the pleura, of the genito-urinary system, the female genital organs (Wolff), the adrenals, bones, etc.; or it is hematogenous in general miliary tuberculosis, or independent of it (Voss, H. Albrecht). Relatively often, in about 10%, tuberculosis occurs with cirrhosis of the liver, usually as a fresh eruption; in some cases the portal of entry cannot be demonstrated, but it may have been very small (v. Hansemann; comp. p. 929); it is believed that the peritoneal involvement is secondary (deficient absorptive power); or that tuberculosis is the common cause of both the cirrhosis and the peritoneal infection (Klopstock). In very old people, the serous membranes are easily infected by tuberculosis (Stahr).

In simple pure tuberculosis of the peritoneum, it shows small scattered nodules.

Pseudotuberculosis (foreign body granulosis) of the peritoneum, caused by ova of parasites which became surrounded by masses of giant cells, has been described by Helbing (ova of tenia) and Miura and Goebel (ova of distomum); the latter mentions nodules of the bowel serosa consisting of hyalin tissue surrounding ova and worms. In larger nodules, Sehrt found ascaris ova, also in small tubercle-like nodules in the omentum and peritoneum. The same reactive inflammatory proliferations appear around oxyuris or their ova which enter the peritoneal cavity from the genital organs through the tubes (Chiari, Schneider, Strada and others, see p. 855), also around particles (lamellae, scolices, hooklets) of ruptured echinococci (hydat.) (de Quervain, Riemann, Deve, lit.); Posselt mentions tubercle-like peritoneal nodules in alveolar echinococcus. After rupture of an ovarian cyst (cf. p. 880), Meyer saw tubercle-like nodules consisting of masses of giant cells around cholesterin plates. More details by Herzog, (lit.). The decidual nodules as found by Walker in ectopic gestation must also be remembered. They start from the connective tissue of the serosa (under the lining cells) and produce large and polymorphocellular, glassy, gray, gray red nodules very like minute miliary tubercles, which in intrauterine pregnancy appear almost regularly from the fourth month onward (Stravoskiates) on the pelvic peritoneum (probably also on and in the ovary, Schmorl), on the ileum, omentum (Penkert), appendix, (Hirschberg), to disappear later, perhaps weeks after delivery, by regressive metamorphosis. More in reference to so-called foreign body tubercles of the peritoneum on p. 882.

But tubercles have abundant giant cells containing tubercle bacilli. There are no noteworthy symptoms of irritation; the nodules are abundant and scattered haphazardly usually in the omentum and mesentery. If very small, they appear like fat lobules of the omentum; later, they are gray, rounded, as though placed upon the membrane. Tuberculosis of the peritoneum is frequently general, but also circumscribed. For histological details in reference to the pathogenesis of tuberculosis of the omentum, see Seifort.

Tuberculous peritonitis is, indeed, rare compared to the extraordinary frequency of tuberculosis in general.

It takes a number of forms:

The most frequent shows adhesions to the abdominal wall, often to complete fusion as the abdominal viscera are united by numerous adhesions. In these red or gray red adhesions, nodules or caseous masses can be recognized; in a small number of cases, there is almost no fluid exudate (dry tuberculous peritonitis), but, as a rule, the spaces between adhesions are filled with serous, serofibrinous, fibrino-hemorrhagic, fibrino-purulent or simple purulent exudate, occasionally, with feco-purulent material from perforations. Fecal fistulae from an encapsulated area may rupture through the abdominal wall. Sometimes everything is so thickly covered with yellow, soft, purulent, fibrinous masses that orientation is almost impossible. The cheesy adhesions are always exceptionally dense between the liver and diaphragm, and around the spleen to the thickness of a finger. The indurated omentum sometimes appears like sausage in front of the intestines, the mesentery may be markedly shortened, and some bowel loops may be almost occluded by kinks and adhesions. The condition is among the most complicated found at autopsy.

In other cases, the ascites presents the striking picture with cloudy, yellow or sanguinous fluid. No adhesions at all may be present, or they may be confined to a few areas; the entire peritoneum, however, especially the omentum, is studded with innumerable, closely placed, gray white or yellow nodules, especially closely crowded near the diaphragm. This is the form found frequently with cirrhosis of the liver. If such patients live for some time, the nodules become illy defined from confluence and are almost hidden by granulation tissue; later fibrous changes wipe out the nodules. In other cases, the nodules show an earlier tendency to confluence and caseation, but are strewn in much granulation tissue. The whole serosa may be slowly covered with a thick layer of brawny, glassy, fibrous or caseating softer tissue, which can be pulled off like a skin. Such cases resemble primary tumors of the peritoneum. Retraction of the omentum and mesentery may occur as in chronic fibroplastic or scirrhus peritonitis. The fused mass of ileum may appear as though covered with a thick fur, and bulge into the abdomen like a globular island.

Tuberculous ascites is often curable by one or several laparotomies during which the exduate is removed. The nodules, rich in giant cells and containing bacilli, undergo necrotic solution to a slight fibrous residue. The factors producing healing are not well understood (Gatti, lit.); recurrence may appear after years, although rarely (v. Winckel). Sometimes healing is spontaneous (animal experiments by Saltykow, lit.).

There are forms of latent tuberculous peritonitis in which the peritoneum is found at autopsy covered with remarkably thick caseous tubercles while the bowel loops are but slightly adherent by transparent organized material; fluid may be completely absent. Some rarer forms resemble bovine tuberculosis in which there are chronic, fibrous peritonitis and round, calcified, cheesy tubercles as large as peas to cherries (like pearls, therefore the name "pearl disease") which hang by delicate threads, or are embedded in the centre of nodules of radiating connective strands. Ipsen described such a case, and the author saw two; in one, a 19 year old girl, fibro-caseous nodules to the size of hazel nuts were found everywhere i nthe peritoneum, often as the centres of threads and strands by which the abdominal organs where glued together. The tuberculous conditions of the peritoneum (also form b) often resemble carcinomatous conditions so closely as to lead to mistaken diagnoses (pp. 878 and 879).

Primary actinomycosis of the peritoneum is very rare (Tiling, lit.). Secondary actinomycosis may accompany actinomycosis of the bowel; perforated ulcers of the bowel cause abscesses or firm tumors. Extensive actinomycosis of the peritoneum is described by Kohler.

Typhoid lymphomas of the peritoneum (see under intestines, p. 794) are gray red, sparse, usually isolated and uneven in size, mostly small, but at times of the size of a pea.

Leucemia.—Occasionally, a thick dissemination of small, white gray or milk white lymphomas resemble carcinoma nodules and tubercles, but are cloudier, more opaque and softer.

Tumors of the Peritoneum

Primary Tumors (Rare).—They are: those rare ones from the actual peritoneum and from the great omentum (Heinsius, lit.), and those which spring from the sub- or retroperitoneal tissues which are far more frequent; but tumors of this kind occur occasionally in the actual peritoneal tissue, usually lateral to the spine; they are solid tumors, chiefly lipomas, most frequently from the mesentery (lit. by Heinricius, Voeckler, Liebermann), or fibromas, myxomas, myxolipomas (the latter diagnosed clinically, Chevalier), leiomyomas (the omentum, J. Richter), sarcomas, *i.e.*, round, fibro- and myxo,- lymphosarcomas, ganglioneuromas (see Oelsner and comp. under nerves) and others. These tumors (lit. by v. Vegesack, Petren) may grow to the size of a man's head and more (weight in a case of Verse, 33.5 lbs.), and are often mistaken for kidney tumors (fig. 426), or cystic ovarian tumors (Martin), especially since they are sometimes soft enough to fluctuate. They are connected solid, or coarsely lobulated tumors with smooth or roughly nodular surfaces; occasionally, smaller tumors are separated from the larger. Females are more frequently affected.

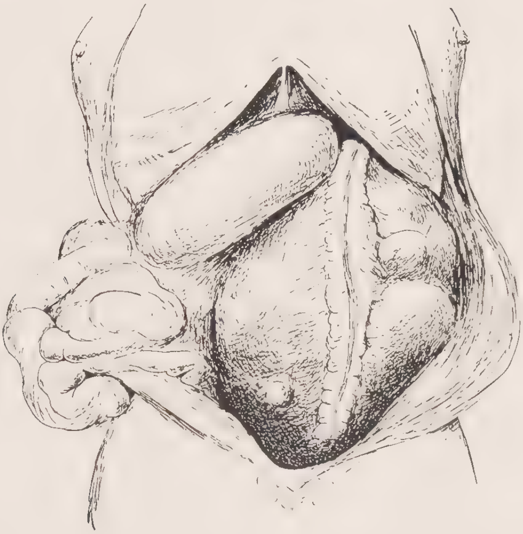


FIG. 426.—Retroperitoneal myxosarcoma of a 25 year old servant girl with pulmonary phthisis. The lateral tumor lifts the flattened descending colon upward simulating a kidney tumor. Stomach displaced upward by the pull of rolled out convolutions of ileum. Cross section of tumor showed fluid center and a thick cortex of firmer tumor tissue (many nodular soft metastases in lungs).

In a case observed by the author (woman 30 years old), a retroperitoneal fibrosarcoma, fluid in the centre, larger than a man's head in size, weighing 6557 gm., filled the inferior vena cava with nodular masses. There was an enormous caput medusae on the abdomen and chest in the last months, edema of legs and genitalia, a long plug extended into the right ureter. The left kidney was lifted upward and lay on the tumor surface in the midline of the abdomen.

Retroperitoneal tumors which spring from the sympathetics must be remembered (see under adrenals). In children, tumors from the structural cells of the sympathetics may be mistaken for hemorrhagic sarcomas

(Berblinger). Median, retropertioneal, cystic, lymphangiectatic tumors are quite rare (v. Haberer, lit.). Occasionally, they are retroperitoneal, in Douglas's cul de sac (Neupert, Walters and Hull, lit.). The author described an angiosarcoma of this region; v. Franque saw a similar tumor which he considered a mesodermal mixed tumor, or "lipoma sarcomatosum" (similar to one described by Borst), and he interprets the "angiosarcoma" of the author as the same sort. In reference to very rare primary mesenteric carcinomas (perhaps from misplaced germinal intestinal anlage?), see Eisenberg; as to solid mesenteric tumors, see Szenes, (lit.). In reference to a malignant adenomyoma of the mesentery, perhaps developed from an embryonal intestinal portion, see Ludwig.

Other rare retroperitoneal, and partly mesenteric cystic tumors, as described by Verocay, Oser (lit.) and others, are designated as adenosarcomas, adenomas, adenocarcinomas, adenocystomas. As high retroperitoneal cystomas, they are clinically well known (Schweitzer); as a rule, they resemble benign ovarian cystomas, even to size (pseudomucinous, multilocular, more rarely serous and monolocular). They grow from one renal region (pararenal) and are circumscribed to the pelvis. They occur mostly in females, but also in males (Obalinski, Helbing, Heyrowsky described a cystoma with carcinomatous degeneration). They are thought to be derived from (*a*) displaced ovarian anlage, or accessory, *i.e.*, ectopic ovaries. (*b*) Since they also occur in males, as the author saw in a case in Basel, persistent, snared-off rests of the anlage of the primitive kidney (the Wolffian body) are believed to be starting points, as discussed by Coblenz (lit. by Schweitzer).

Even in children, there appear in the mesentery, cystic, rarely cavernous (Takano-Hanser, lit.), lymphangiomas which sometimes have chylous contents (chylangiomas, so called chylus cysts). They are like bladders, uni- or multilocular, thin-walled, commonly called mesenteric cysts and may contain several litres of serous or chylous fluid (lit. by Penkert, Klemm, Tugendreich, Kostlivy, Hubner, Hinz, Junghanns, Bolognesi, lit., Rona, Poulsen, Palmowski, Kuster). Most of them appear in the mesentery of the small bowel. Very often a loop of bowel grows over the anterior cyst wall and may be mapped out by percussion (tympanitic sound) from the flat surroundings; it causes a furrow in the cyst wall. See intestinal cysts, p. 727.

Multiple cystic lymphangiomas, lymphangioendotheliomas of the peritoneum (and pleura, Henke) without inflammatory changes, sometimes also retroperitoneal, are very rare (Ernst, Nager, lit., Karas, lit. Himmelheber, Moser and Ricker, lit.) and difficult to interpret (Roegner, Firket, lit.). In an endothelioma of the peritoneum, Borst saw multiple endothelial cysts snared off. There also occur multiple, small, up to fist size lymph cysts or lymphangiectasias due to chronic inflammation of lymph vessels in chronic peritonitis. The author saw the condition in a 60 year old woman with chronic peritonitis, zuckerguss liver and splenic tumor (see Harbitz, who saw chylous ascites), also in tuberculosis of the peritoneum with chylous ascites. Cysts to the size of a chestnut, of efferent tuberculous lymph vessels within the area of tuberculous intestinal ulcers are described by Geipel. The author has seen such cysts. Cystic degeneration of lymph nodes are also classed with lymph cysts (lit. by Odenius, Smoler, Elter and cf. p. 175). Cavernous hemangioma of the mesentery with occlusion of the bowel is described by Julliard, Mariani.

Dermoid cysts, uni- or multicystic, up to the size of a man's head, occur; cystic teratomas (with fetal inclusions) occasionally reaching the size of a man's head even in the newborn, and other mixed tumors occur in the omentum, (Conforti), mesentery (occasionally also in the abdominal walls at the umbilicus, Cornils, lit.), retroperitoneal and high (Ruge, lit., Sand and Lerat, Lohr), in the pelvic connective tissue (Arzt, lit.), and in the vicinity of the ovaries (Lexer, Winkler). From lining cells, snared off by peritonitic processes, there may originate gland-like structures and cysts. Pseudocysts can be formed by the enclosure of exudate between inflammatory membranes. Blood cysts occur (rare), *e.g.*, in the mesentery, derived from hematomas or chylous cysts (Junghanns, lit.).

Inflammatory mesenteric tumors have lately received attention. They reach the size of an apple, are firm, consisting chiefly of vascular granulation, and connective tissue and occur on the mesentery of the small bowel and colon. The author has examined such cases (lit. in appendix); in one, an attempt at extirpation of the "tumor" which was attached close to the mesentery, had caused fatal gangrene of the bowel and peritonitis. They are probably genetically closely related to the "inflammatory tumors" of the omentum which appear mostly in the form of solid, smooth, or slightly nodular, firm, circumscribed tumors (Schnitzler, Braun) and which occur postoperatively (local infection) as also in inflammation of adjacent organs (thrombotic, embolic circulatory disturbances in hernias!) (Zesas, lit., Hollander, epiploitis plastica, Schmieden, Peterhanwahr).

In reference to cysts with ciliated epithelium, see p. 880. Firket described as "maladie kystique" numerous cystic tumors anywhere in the peritoneum, especially the omentum, which spring from peritoneal epithelium. Hueter described "inflammatory gland-like new formations of the peritoneum" in the serosa of the bowel, which also grow into the musculature, and he speaks of "adenoid peritonitis" (see also adenomyomatosis, p. 806).

Primary peritoneal tumors are distinguished by their extension over the whole peritoneum following the course of the lymphatics, as well as by the appearance of quantities of ascitic fluid, frequently deep red; when larger amounts of fibrin are added, the fluid takes on the character of an exudate.

Tumors derived from actual peritoneal tissue are:

(*a*) Endotheliomas, from the endothelium of the lymphatics and lymph spaces (lymphangioendotheliomas) with characteristics similar to those of the pleura (p. 492).

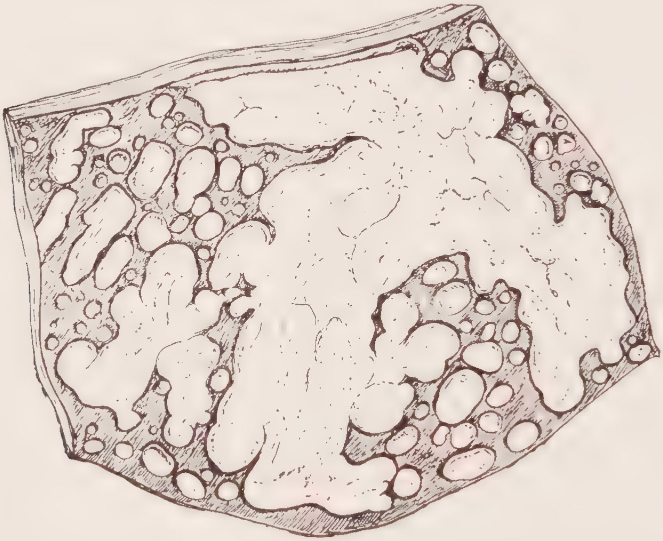


FIG. 427.—Primary peritoneal tumor (endo- or mesothelioma) derived from the lining cells. Piece of lower surface of diaphragm. The peritoneum was covered everywhere with similar soft tumors, partly caseous, which in some places were 1 cm. thick, but usually more flat, and formed an often coherent caseous layer on the bowel loops. The omentum was as thick as a thumb, infiltrated by innumerable nodules and adherent to the bowel loops. Hemorrhagic serous fluid in abdomen. Woman 27 years old, sick for 6 weeks with clinical symptoms of peritonitis.

It may happen that a primary tumor of the pleura extends to the peritoneum by continuity (p. 494), and the serosa of the liver is covered with a layer of the neoplasm. Miller and Wynn described a case with mucoid ascitic fluid. See also Scholer.

(*b*) Tumors which originate from the single layer of cells which line the body cavity.

The names in common use are: endothelioma, mesothelioma, carcinoma (see a. o., Eisenberg, Yamane), malignant lining-cell tumors or malignant serosal epitheliomas (Herzog), consult pp. 493 and 179.

The tumor illustrated in fig. 427 formed innumerable, flat, button-like nodules and plaques, which frequently formed larger low plateaus by confluence. The tumor tissue was of soft medullary consistency, white and caseated and yellow, very closely resembling caseous tuberculosis. Microscopically, the character could not be recognized in caseous nodules, but in well preserved places there were nests and strands of large angular cells, some cylindrical and arranged in palisades, all in a fibrous vascular tissue. The lining of the peritoneum in places where there was no tumor, was also thickened in multiple layers.

Primary diffuse cylindrical cell carcinomas, changed into mucoid carcinomas, have also been observed; it is believed they originate from embryonal, snared off parts of intestinal anlage (Birch-Hirschfeld, see also Rosenbach) or from the lining cells themselves (Kirchberg).

(*c*) Sarcomas (sarcomatosis) of the peritoneum are very rare.

Some are plexiform angiosarcomas consisting of newly formed vessels, from the adventitia of which proceeds a mucoid tissue proliferation. They may then resemble mucoid carcinomas macroscopically (Waldeyer; Tarozzi). Other forms are presented as peritheliosarcomas, as in a woman 40 years old with very marked ascites, recurring after paracentesis. The whole peritoneum was covered with fibrin, below which the serosa was thickly covered by small, warty, plug- or comb-like nodules, but also flat, less distinct, moderately firm, gray red and extremely vascular masses. In a man 66 years old, the author saw the peritoneum thickly studded with innumerable light gray to gray red nodules reaching the size of a pea; they often coalesced into plaques; microscopically, it was a very polymorphous large cell sarcoma, but without a trace of alveolar or epithelial arrangement. Ernst Fraenkel and the author described a case of soft vascular myxosarcoma from the omentum; numerous metastases had spread to the whole peritoneum; many of the soft, transparent closely packed tumor nodules were pedunculated and suggested grapes. Dionisi saw pedunculated nodules of a vascular, spindle cell sarcoma in a 50 year old man. In a man of 53, the author saw spindle cell sarcomatosis in the form of plates and nodules on the peritoneum with an omental tumor as large as a fist. Motzfeldt (lit.) described a fibrosarcomatosis. In a 29 year old man, the author saw an omental tumor (vascular spindle cell sarcoma, 3640 gms. in weight), nodular, firm, veins on its surface as thick as a thumb, and adherent to loops of the small bowel. Sarcomas and mixed tumors, rhabdomyosarcomas, of the omentum described by Conforti, lit. Billigheimer saw a primary lymphosarcoma of the omentum.

Secondary Tumors.—Those most frequent are carcinomas; a purely nodular, carcinosis peritonei can be differentiated from a peritonitis carcinomatosa which is tumor development accompanied by an exudative, mostly serofibrinous inflammation, similar to that in tuberculous affections. There are transitions between these two forms.

The primary tumors of secondary carcinomas of the peritoneum are in the stomach, the flexures, gall bladder, ovaries. The extension is often rapid, as in an inflammation. Frequently it occurs by dissemination and tumor masses are found in the deepest places, *i.e.*, in the hypochondria, the rectouterine and rectovesical spaces (so-called metastases of Douglas), but occur at any place, thus in the angle between the mesentery and bowel, at the mesenteric attachment, etc. Metastasis may occur via the lymphatics (comp. under intestines, p. 823), or by grafting (Tilp, Misumi), from a reactive inflammation and a sort of organization of tumor particles; but, according to Kraus, cells may pass through the stomata (see p. 859) between the lining cells into the peritoneal tissue. In other cases, extension is by continuity, or in apposing areas by contiguity according to the modes mentioned. The largest rounded nodules are found in the lower abdomen, the sides of the abdomen and toward the mesenteric root. The nodules in the hypochondriae are naturally flatter. Marked ascites is present before the carcinomatous change, or is caused by the carcinoma. The fluid is cloudy serous and often hemorrhagic.

The various forms of secondary carcinoma of the peritoneum produce diverse pictures. Scirrhous carcinoma (most frequently from the stomach) extends diffusely, is accompanied by marked contraction, and much ascites; it often fuses the loops of the small bowel into a hard ball no larger than a fist (the English have compared the picture to a "rose") pulled firmly to the spinal column by the shortened, retracted mesentery; the omentum lies as a small, hard, cylindrical structure between the transverse colon and stomach. In other cases, scirrhus forms result in multiple, flat, indented, contracting nodules in the omentum and mesentery, especially in the recesses of the attachment to the bowel, or in innumerable miliary, hard nodules, resembling tubercles, or in diffuse, contracting and disseminating carcinoses. The resemblance to tuberculosis is always present. Soft, cellular adenocarcinomas usually produce nodular metastases which favor the line of attachment of mesentery and bowel, the sides of the abdomen, the diaphragm and the recto-vesical and recto-uterine spaces (metastases of Douglas). In psammo-carcinoma from the ovaries, the nodules have a sandy feel. Diffuse mucoid carcinomas, most frequently from the stomach or the gall bladder, produce voluminous tumor masses, especially around the stomach, transverse colon and omentum, but glassy, yellow or yellow red tumor masses are everywhere, consisting of a honeycomb-like fibrous network filled with gelatinous material; in fact, the thick tumor masses may infiltrate the whole peritoneal membrane. There frequently are encapsulated spaces filled with yellow or red fluid. The omentum usually bears the brunt of the changes (carcinoma in its lymph vessels by Suzuki, comp. J. Koch), and becomes a flat, cake-like or cock's comb-like tumor, scirrhous, shortened or turned upward, glassy, thick, cylindrical, between the stomach and transverse colon. Nodules may be found which are still white, opaque, somewhat more firm, showing only beginning mucoid metamorphosis (p. 704). Diffuse soft medullary carcinomas are more rare; they produce distinct lumps. In carcinomatous infiltration the lining cells may react by proliferating independently (Borst).

Seifert cautions against mistaking certain white nodules of the omentum for carcinoma nodules (fat, clumps of wandering cells, etc.).

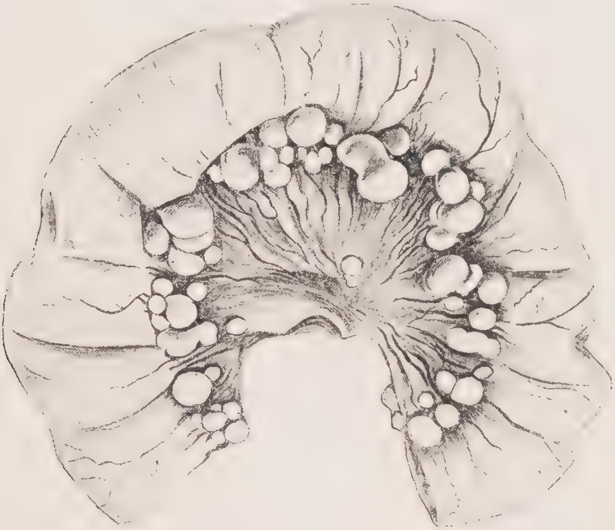


FIG. 428.—Numerous metastatic sarcoma nodules in mesentery near the attachment of intestines from primary melanotic sarcoma of choroid membrane (eye removed 1 year before) of man 48 years old. Innumerable metastases in almost all organs, gastric and intestinal mucosa, gall bladder, prostate and left epididymis. Some nodules melanotic, others colorless (see under liver); ⅔ nat. size.

Isolated carcinoma nodules have been observed in puncture openings, and inoculation is believed to occur.

Sarcomas are rarer, chiefly melanotic, favor the mesentery and its attachment to the bowel, generally fungoid, or globular and have smooth surfaces (fig. 428). Some ovarian tumors, even benign and not carcinomatous or sarcomatous, may metastasize in the abdominal cavity. Arborescent growths break through a tear in an ovarian cyst and cover the peritoneum with papillae similar to those which line the cysts. It is assumed that the implanted epithelium, continuing to proliferate, forms hollow spaces, and thus is explained cases in which the vicinity of the ovaries and the serosa of the uterus were covered with innumerable, small, smooth cysts, lined with ciliated epithelium as described by Pfannenstiel and others. In reference to other cysts in this locality, see chapt. cysts—ovaries; for implantation nodules in ovarian dermoid cysts, see there and below.

The rupture of a colloid adenocystoma has been followed by acute peritonitis, or by so-called "peritoneal pseudomyxoma" (Werth), or, according to Kuster, mucoid abdomen or gelatinous ascites. The mucoid substance is covered by the reacting proliferating peritoneum, and organized, thus becoming more or less fixed and circumscribed into clumps or gelatinous cysts. Others (Olshausen, Santlus, Sitzenfrey, Schumann) believe these "pseudomyxomas" are implantation metastases of ruptured cystomas. This epithelium and not the escaped mucoid material plays the essential role, according to the investigations of Eug. Fraenkel. But it is certain that the epithelium may lose its faculty of producing mucus (cases of cured peritoneal pseudomyxoma) and it may be assumed in some cases that the escaped epithelium adds very little to the mucoid material (Goldschmid, lit.). Werth's conception applies to these latter cases. Marchand accepted it for his case, see also Wilson.

A similar picture may develop in males if the mucoid contents of a ruptured hydrops of the appendix escape into the abdominal cavity, although it does not have the progressive, clinically dangerous character of a peritoneal pseudomyxoma from cystoma (Eug. Fraenkel, Hueter, lit. Goldschwend, Tarozzi, Neumann, Honecker, Mercier-Bellevue, Muller, Comolle, lit., Lignac, Michaelsson and lit., p. 839). The peritoneum reacts with "foreign body peritonitis." Merkel describes implantation of escaped intestinal epithelium into the abdominal cavity, analogous to the implantation metastases of cystomas, but Eug. Fraenkel considers Merkel's case an exception, and believes contrary to what occurs from epithelium of ruptured cystomas, that the cylindrical epithelium of the ruptured appendix as a rule does not undergo any noteworthy increase (emphasized by Oberndorfer). Rogner saw peritoneal pseudomyxoma after rupture of an enterocystoma (p. 727), Walz in aseptic fetal perforative peritonitis.

Just as in spontaneous metastasis, a common benign glandular ovarian cystoma may cause metastases by the implantation of detached tumor cells during its operative removal. Indeed, the tumor portions are supposed to be sources of recurrences of a malignant character. Of course, scepticism should be practised; probably the primary tumor was already carcinomatous (Milner, lit. Polano). Kolaczek, Schroder, Herzog (lit.) and others, (lit. by Koch) saw the contents of dermoid cysts of the ovary spilled in the peritoneal cavity with the continual development of structures, some solid, some cystic, but all containing dermoid material.

The laparotomy scar is a notorious place for lymphogenous metastasis after extirpation of carcinomatous genitalia. The assumption that these are implantation metastases is not proven (Raabe). Amos and R. Meyer saw adenomatous proliferation of epithelium of the serosa in abdominal scars after fixation and disturbance of uterine adhesions. The theory of Franz that this is a seeding of parts of uterine mucosa during operation is rather improbable.

Foreign Bodies and Free Bodies, Corpora Libra

These may enter from without, such as bullets, needles, etc., which passed through the stomach, urinary bladder, abdominal walls, etc., or may be gall stones, fecoliths, freed by perforations, fetuses, freed by rupture of the uterus, or developed in the tubes (later a lithopedion), detached subserous myomas of the uterus which reach the size of a goose egg and become externally calcified, detached, pedunculated tumors of the ovary, stomach, intestines or separated egg-shaped or globular, rounded and structurally more or less changed lipomatous appendages epiploica (p. 807), or pedunculated lobules of the omentum. The two latter forms represent bodies (corpora aliena adiposa) consisting of soft necrotic or fat material surrounded by a fibrous capsule; if they calcify, they become like beads (p. 491).

The structures, specifically called "corpora libra" are rare, usually small (exceptionally as large as a hen's egg, Hoche, lit.), white, yellow, transparent or cloudy, smooth, oval, round or flat, often with lamellated structures, hyalin lustre, consisting of fibrin and analogous to the rice bodies of tendon sheaths and joints. The author saw secondary adhesion to the mesentery.

If small sterile foreign bodies enter the peritoneal cavity, *e.g.*, threads from a sponge, or an entire sponge or an iodoform gauze packing, they are surrounded and permeated by foreign body giant cells; the smallest fibres are enclosed in nodules resembling tubercles (Kaspar). Pressure necrosis may allow a whole gauze compress to enter the bowel, bladder or vagina (Hinterstoisser, lit.). Hanau and Brandes after escape of gastric contents in peptic ulcer, Askanazy and v. Gyergyai after a tear of the intestines and escape of feces, saw peritoneal nodules consisting of giant cell containing granulation tissue enclosing vegetable cells. (Comp. the experiments of Podwyssoski with infusorial earth; see Herzog, lit. later work in reference to imbedding processes in the peritoneum.) Escaped meconium may become hardened by calcium salts into concretions embedded in the peritoneal cavity (Dubler, Askanazy). Comp. p. 870 in reference to so-called foreign body tubercles around parasitic ova, especially oxyuris, etc.

Parasites

Echinococci appear primarily as single or a few examples, but may produce enormous sacs which become adherent to their surroundings;

they favor the cellular tissue under the peritoneum of the pouch of Douglas and may rupture into the rectum, bladder, uterus, vagina; they also may impede child-birth (Gussakow). Secondary multiple echinococci of the abdominal cavity develop by dissemination of a ruptured echinococcus cyst, almost always from the liver. The engrafted daughter cysts, or liberated embryos (scolices) may in turn actively enlarge. The author saw a very rare enormous dissemination of echinococcus in the abdominal cavity from echinococcus cyst of the liver in a 23 year old girl (described by Grumme, illustrated). Such implantations in the peritoneum and even in the abdominal wall, may occur at operation (Madelung). More details as to rupture of an echinococcus cyst and its consequences in the abdominal cavity on p. 977, under liver.

It has been mentioned (p. 852) that an ascaris lumbricoides may accidentally pass through a perforation of the bowel into the abdominal cavity. Oxyuris, see p. 854. Cysticercus and pentastomum are rare (see p. 978, under liver).

Coccidium oviforme, a parasite belonging to the sporozoa, frequently causes tumor-like epithelial proliferations in the bile channels of rabbits, but is rare in man (in the small bowel or liver). The author saw large numbers in the clear brown yellow contents of a small, thin-walled, flat cyst in the serosa of the diaphragm above the stomach.

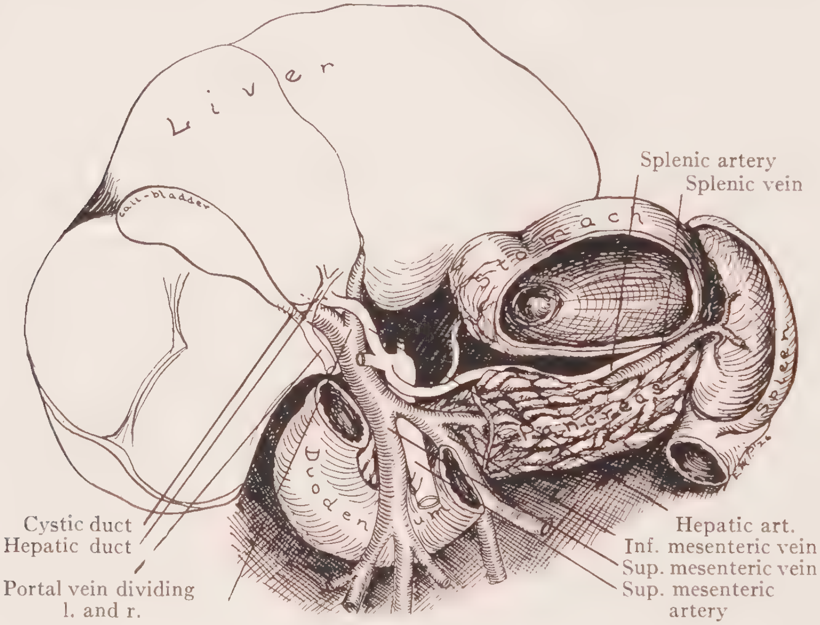
THE LIVER

The liver develops, according to Hertwig, from net-like, branching, tubular glands by the growth of two hollow cylinders from the duodenum, the anlage of the future right and left lobes which penetrate the ventral intestinal mesentery. Solid side branches, liver buds, grow from the hollow cylinders and soon intermingle, some producing bile passages and some liver parenchyma and its bile capillaries.

More recent investigations modify this view. From budding and progressive pushing out of primary liver diverticulae, *i.e.*, bile duct anlage, the bile ducts of larger calibre alone are developed, while the liver parenchyma grows from solid cell masses found very early on the ventral and anterior walls of the liver diverticulum. The cells of this mass actively multiply and are arranged into anastomosing cylinders, the liver trabeculæ; from these, certain cell strands which envelop a lumen finally develop into the smaller and smallest periportal bile passages (Lewis). The connective tissue of the liver is mesenchymal in origin, while the remainder is a product of the entoderm.

To understand the structure of the liver, a subject not as yet completely elucidated (see Kretz, Gilbert-Villaret, Bauer), it is perhaps best to begin at the hepatic veins which receive blood from the capillaries and carry it through 8 to 10 main branches into the inferior vena cava. If we follow these veins backward, we find that they branch into larger vessels, the sublobular veins, within the substance of the liver. The latter course between the so-called lobules on one, somewhat flattened, side, *i.e.*, the bases of the liver lobules; smaller uncovered branches arise form these and penetrate the parenchyma. The sublobular vein is formed by the union of a number of central veins. The latter in their turn travel in the long axis of the so-called acini, or better, lobules. The lobules themselves are barrel- or egg-shaped and consist of a network of branching strands of liver cells, and liver columns or cords which surround the central veins like a thick collar. On cross section, the lobules are about 1 mm. wide, irregularly polygonal, and contain the central veins in their centres. The angular, usually three cornered, prolongations of Glisson's capsule with their embedded ducts and vessels, are seen on the edges. The gland cells, *i.e.*, the liver cells proper are polyhedral, cubical, with granular protoplasm, eccentrically placed nuclei, perhaps multiple, and nucleoli. (For more detailed description, see Rathery, lit.) A network of very fine capillaries occupies the spaces between the columns of liver cells. On transverse section of the lobule, the capillaries are arranged radially toward the central vein. These capillaries possess certain peculiarities of their own. There is no well formed tube lined by narrow, closely approximated endothelial cells, but every so often there is a branched cell in the walls which juts into the lumen on the one side and is insinuated between liver cells on the other side. This is a special form of capillary endothelial cell which is called Kupffer or star cell, possessing, among other properties, marked phagocytic powers. Between the blood capillaries and liver cells there is only a reticulum, and since the liver cells do not lie on a membrana propria, there is, as Schaffer points out, very little hindrance to the passage of metabolic products between cells and blood. This intimate intermingling of the double network from liver cell columns and blood capillaries is said to be characteristic of liver parenchyma (Geraudel). The extensive, dovetailed capillary system results in a very slow circulatory rate. The network is fed by the portal vein and connects the central veins with the vessels distributed between the acini. The latter two are the afferent vessels, the portal vein which is the functional and larger, and the hepatic artery, the nutritive vessel. Both enter the liver at the hilum and course between the acini. Larger branches of the main portal trunks can be seen on section where three or four liver lobules touch. These are interlobular veins and from them smaller branches run between each lobule, ultimately to empty their blood through the intralobular capillaries into the central veins. (For a consideration of the independence of liver lobules or their double blood supply, see Hess.)

Translator's Remarks.—In the dog, the splenic vein joins the superior mesenteric vein at a right angle, so that most of the blood from the splenic vein reaches the left lobe of the liver and more blood from the superior mesenteric vein reaches the right lobe. Apparently there are two streams, that coming from the splenic vein pushing the other against the right wall of the portal vein until the division into right and left is reached, whereupon the two streams take their respective directions with little intermingling, analogous to the condition of the Mississippi River for some distance below where it is joined by the Missouri. In the human, the angle is more obtuse so that intermingling is better; nevertheless, more blood from, say, the ileo-cecal region, reaches the right lobe than the left (amebic abscesses in right lobe; secondary liver abscesses from appendicitis more numerous in right lobe,



Anterior view

FIG. 429.—Diagram showing the blood supply of the liver and the spleen, especially of the portal vein. It is known that amebic abscesses are much more frequent in the right lobe than in the left, and that certain types of cirrhoses begin in the left lobe and are always more advanced in that lobe. From the diagram it can be seen that most of the blood going from the splenic vein will pass into the left lobe of the liver and most of that going from the lower intestinal tract will enter the right lobe of the liver. It is analogous to the muddy stream on the one side of the Mississippi and the clear on the other, below where the Missouri empties into that stream, hence infection, etc. from around the ileo-cecal valve, for example, will pass more to the right lobe than to the left. Toxins, etc. from the spleen will be sent in larger quantity into the left lobe than into the right. In the dog the angle made by the splenic and superior mesenteric veins is more of a right angle and it is possible to quite sharply divide material injected into either one or the other of these veins into the right and the left lobes. L. H.

etc.). See: Independence of Lobes of Liver; Bartlett, F. K., Corper, H. J., Long, E. R., Am. J. Physiol., 35:36, 1914.

The artery breaks up into a capillary network in the periportal tissues from which venules arise emptying into the interlobular veins, hence the name, portal roots; from these the blood flows through the intralobular capillaries and thence into the central veins. There are thus direct communications between portal vein and hepatic artery. Since the arterial blood, now venous, is also collected by the central veins, the latter are the efferent vessels of the organ.

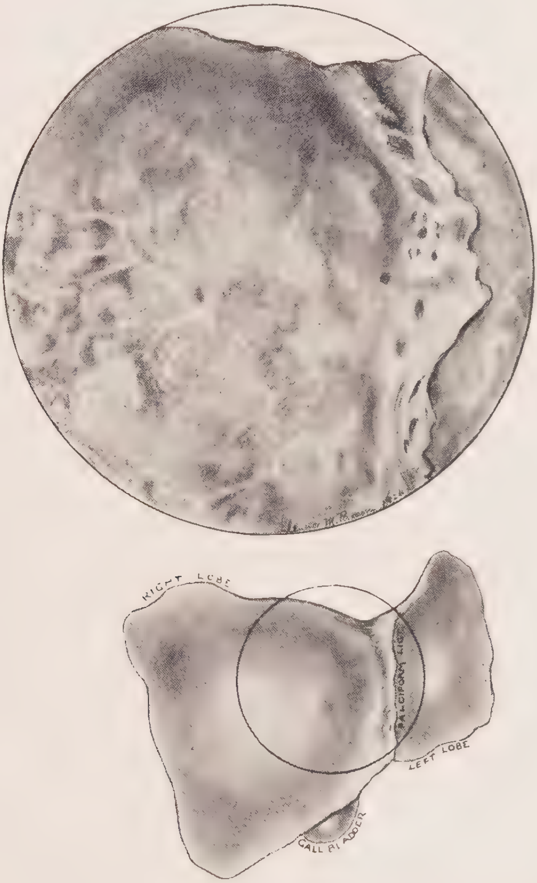


FIG. 430.—Injection of the lymphatics in multiple abscesses of the liver. Superior surface. From a patient 38 years old. Many abscesses were present throughout originating in a suppurative cholecystitis and ascending cholangitis. It is remarkable because of the fine tracery of lymphatics as shown. Each of these lymphatics, when sectioned, was shown to be swollen and filled with pus cells. Such preparations yield important anatomic data. L. H. #165.

Bile, as elaborated by the liver cells, first enters the bile capillaries or canaliculi. Tiny canals in the liver cells themselves have been described by Noel Fiessinger (lit.). The intralobular canaliculi are nothing but cylindrical spaces between the cells, formed by a furrow on the cell surfaces which fits correspondingly with that of its neighbor. The canaliculi are collected at the periphery of the lobules and form the interlobular ducts which are structures with walls of their own, lined at first with low and then higher cylindrical epithelium. According to Lewis, they develop from liver cell trabeculae. The larger bile ducts, again according to Lewis, develop from special anlage. As the ducts grow larger they contain more and more connective tissue and smooth muscle in their walls, and those of the large ducts have small mucous glands within them. The smaller passages anastomose very freely.

Connective tissue is quite sparse in the liver and elastic fibres are relatively few in number. The organ is covered by Glisson's capsule, from which prolongations enter its substance and form sheaths for the interlobular system of tubes (portal vein, hepatic artery, bile ducts and numerous lymph vessels). In the lobules themselves, only traces of connective tissue are arranged between the capillary endothelium and the columns of liver cells demonstrable by the use of special methods, (Mallory, silver impregnation); they are present intermingled as networks around capillaries and as radially running single fibres (see also Maresch, Kon, Hueck, Huzella).

Lymph vessels are particularly numerous and may be seen to good advantage when distended as by carcinoma cells. The network of lymph vessels in the peritoneal covering communicates with the interlobular system. Vessels also run along the portal vein and in its wall, along the artery, in the adventitia of the hepatic veins and in the walls of the bile ducts. Between the liver cells on one side and the blood capillaries on the other, there are said to be lymph spaces devoid of endothelium, but surrounding the intralobular blood capillaries like a sheath (Disse). Their existence is denied, however, by Browicz, Hering and Simpson, but affirmed by Reinke and others. Eppinger, Jr., believes there are lymph spaces between Kupffer's cells and liver cells. According to Teichmann, there are no lymph vessels at all within the liver lobule. The author knows there are spaces between capillaries and liver cells because edema fluid collects in this position and, according to Hueck, it lifts the liver cells from the reticulum and clearly defines the spaces; amyloid is deposited in this situation and cell masses collect there in the leukemias. Shaffer says the reticulum encloses a system of spaces which must be of the nature of lymph vessels because injection fluids communicate from them with the interlobular lymph vessels.

Non-medullated and a few medullated nerves are found, especially in the connective tissue.

The lobules can be seen by the naked eye, and it is customary to distinguish a central zone bordering on the central or hepatic vein, and a peripheral zone bounded by Glisson's capsule. The central zone is usually darker than the peripheral. A middle zone is also recognized, between central and peripheral zones, ordinarily not well differentiated. To become oriented on section of the organ when numerous vessels are cut, observe: the hepatic vein is alone, an opening is seen lined by the delicate wall of the vein, the smallest branches are directly surrounded by parenchyma without connective tissue in the neighborhood. The portal vein is embedded with the bile ducts and hepatic artery in Glisson's capsule. The central veins can not be seen by the naked eye; the lumena of the smaller portal branches appear as fine streaks in Glisson's capsule.

The weight of the liver in adults is about 1500 grams, with considerable latitude, (see Rossle). At birth it weighs about 120 grams, or 4% of the body weight. Its longest diameter varies from 25 to 30 cm., height 20 to 22 cm., thickness 6 to 9 cm.

Post Mortem Changes

Decomposition sets in quite early from the invasion of bacteria via the bile passages and portal vein, particularly in septic deaths in which decomposition on the whole is rapid. The liver is stained dirty brown and blue in the neighborhood of blood vessels.

Bacteria, particularly colon bacilli, are said to invade the blood from the intestines even during the agonal period (animal experiments of Wurtz, Beco, Chvostek and Egger). The liver is said to be invaded during the agonal period also via the bile passages (Achard and Phulpin). New and better methods have shown, however, that such early invasion is uncommon (Simmonds, Canon, Dilbelt).

Emphysema in advanced decomposition makes the organ spongy and crepitant on section, later semi-fluid and soupy. Occasionally, leucin and tyrosin separate from decomposing livers in the form of a white, mouldy coating (see p. 908 under acute atrophy, and p. 913 phosphorus liver). The surface, particularly the lower border, is often blue black in the body, and in the presence of purulent peritoneal fluid this may actually begin while the patient is still living, due to the formation of a sulphur-iron compound, (see p. 659); it may extend several millimeters into the parenchyma. It is termed pseudomelanosis, in contradistinction to melanosis which does not give an iron reaction.

Occasionally, gas-forming anerobic bacteria produce huge gas-filled blebs and a veritable emphysema before the ordinary post mortem changes have begun. The process is quite similar to that occurring in the skin (skin phlegmons), or in the uterus of puerperal fever. In an extraordinary case reported by Ernst, the section surface was covered with colorless foam (schaum leber). This particular change has been obtained experimentally during life by W. H. Schultze; Ghon and Sachs may be consulted for details of its etiology which is not uniform.

Not rarely there are seen on the surface of the liver, (*a*) flat, bright yellow, circular or striped spots, extending more or less deeply into the tissue and poorly demarkated. They represent areas made anemic by the pressure of surrounding parts such as coils of bowel, stomach, ribs, etc. Of slightly different nature are (*b*) the characteristic sharp cornered, pale yellow areas somewhat wedge shaped, or pointed or angularly circumscribed, usually not deep in the interior, also occasionally seen in the parenchyma near the capsule. Their shape excludes the assumption of an anemic process. Helly believes they are of septic origin, a focally distributed edema, and points out that they are grouped about the branchings of the portal vein and hepatic artery. Beneke concludes they are caused by agonal vessel spasms which may occur without sepsis. They are seen particularly often in acute cerebral disorders and acute peritonitis.

Anomalies in Shape

These may be congenital or acquired. Abnormal lobulation is not rare; pedunculated polypoid structures are seen from the size of beans to hazel nuts, or furrows are found in the sharp edge of the liver, especially its right lobe. This lobulation is congenital or is caused by connective tissue proliferation and subsequent cicatricial contraction. Calloused contractions on the surface of the liver may be of traumatic origin. Abnormal lobulation sometimes leads to the formation of one or more accessory livers which have been found in the great omentum and in the suspensory ligament (Tarozzi). The author saw a small accessory liver on the apex of the gall bladder (see Ribbert). [For description and lit. see also, Cullen, T. S., Arch Surg., 2: 718: 1925.—*Translator*.]

Occasionally, abnormal lobulation is seen in umbilical or diaphragmatic hernias (see form anomalies with congenital hernias, p. 890). Sometimes a congenital disproportion of the lobes is present in which a main lobe is abnormally small or hypoplastic. In one of the latter cases, the author saw the gall bladder situated at the right edge of the liver. The other parts undergo compensatory hypertrophy (lit. by Kantor). Other acquired form anomalies will be mentioned under the several diseases of the liver.

Changes in form produced by pressure are very frequent. Pressure can cause atrophy, or only a change in the external shape of an organ soft enough to be remodelled. Pressure effects frequently observed are furrows on the liver surface running in various directions (see fig. 465). There may be:

(*a*) A deep furrow, broad, almost horizontal, or slightly oblique passing over the anterior convex surface of both lobes, a frequent effect of too tight fitting garments, especially corsets (the typical transverse lacing furrow). In lacing, the lower part of the thorax is compressed and deformed, the liver is forced downward, and the edge of the rib border is forced deep into it. The capsule is slightly thickened in this compressed area (perihepatitis). The liver parenchyma is frequently atrophic and reduced to a white layer which gradually changes into a thin fibrous bridge connecting the upper main part of the liver with the part snared off. The latter shows venous congestion and in conjunction with compensatory hypertrophy may become thickened and rounded; occasionally it is three or four cornered. This snared off portion may become so mobile that it turns upward, (flap-liver), or, in other cases, may be mistaken for a floating kidney. The gall bladder is attached to this snared off right lobe. If the neck of this organ and the cystic duct happen to be compressed, there is stasis of bile in the gall bladder which favors calculus formation. Pulling of the cystic and common ducts may cause occlusion and icterus (Virchow). In old men, a transverse pressure furrow is sometimes caused by an unyielding thorax. It may also occur from pressure of the costal arch in kyphoscoliosis.

(*b*) When the liver is very large or when the lower part of the thorax is much constricted, approximately parallel, arc-like impressions of the ribs may be seen on the right lateral margin.

(*c*) Sagittal furrows on the upper convex surface, two or three in number and usually parallel, may be congenital (Orth), or acquired from difficult respiration as in emphysema, or by lacing. According to some opinions, pressure effects may be exerted by thick rolls of hypertrophic muscle attachments of the diaphragm. Quite frequently it can be demonstrated that cylindrical swells of diaphragm fit into these furrows (diaphragmatic furrows, Zahn). Others think the diaphragm is folded because of difficulty in expiration (Liebermeister), or from lacing, *i.e.*, narrowing of the lower thorax (lit. up to 1905 by Moody). Chiari believes the essential factor is an intrauterine pressure of the liver against the diaphragm, the muscle bundles of which are forced apart and form folds, or hypertrophy. Both means may press furrows into the liver. In adults, main causes are the blows of coughing, which violently and repeatedly force the liver against the diaphragm. Walz speaks of bending furrows caused by flattening of the diaphragm and the liver surface. Westenhofer calls them congenital space folds, the liver being forced into folds by a too narrow space in which the diaphragm must adapt itself. In these sagittal folds, the pressure may be slight enough to give the impression that the soft, almost pliable liver substance has simply been squeezed away. There is practically no perihepatitis.

Sometimes other impressions, explained by the pliability of the organ, are seen without atrophy. It may be caused by a superimposed loop of intestine, by exudates, even gases alone (in intestinal perforation), may compress the liver deeply (comp. subphrenic gas bubbles and the subphrenic gas abscess of the surgeon— Liebmann and Schinz, lit.).

Changes in Position

In situs inversus, the liver occupies the left side. Displacements downward, upward and sometimes obliquely, may be caused by filling of the pleural cavity or the abdomen by exudates, tumors, meteorism, etc. Floating liver is caused by extension of the suspensory and the coronary ligaments. The displacements by lacing have been mentioned. The entire liver, a whole lobe, or outstanding parts of it, may enter umbilical, funicular or diaphragmatic hernias and show deep, almost fibrous constriction or pressure furrows.

Circulatory Disturbances

(Within the hepatic veins)

Congestion of the Liver.—Passive congestion of the liver from cardiac lesions (foie cardiaque), and respiratory disturbances is a very frequent contingency, for the hepatic veins are involved early in general circulatory disturbances due to their proximity to the heart. The central veins and the nearest capillaries are dilated first. In the beginning, the liver is often enlarged, and the capsule is under tension; the surface, and more so, the section surface, show the acinar etching very clearly and regularly. The central parts are dark red and sharply outlined from the peripheral parts which project slightly on the section surface and usually, because of fat infiltration, are of light brownish gray to yellowish color. The organ may be somewhat enlarged. If the congestion increases (second stage), the peripheral parts of the lobules are involved so that the red areas visible on the section surface enlarge, may blend with each other. This congestion causes pressure atrophy of the columns of liver cells lying between the dilated capillaries. The single liver cells become small, pigmented (fig. 436), and may finally disappear entirely with the exception of small pigmented remains. The whole lobule may be involved. The organ becomes smaller, very vascular, darkly pigmented and on section looks somewhat like a nutmeg (nutmeg liver, cyanotic atrophy). The weight may fall to 1000 or 750 gms. When atrophy supervenes the congested areas appear sunken, and since they finally reach to the periphery, the deeper lying dark areas starting from the centers of neighboring lobules pass toward each other with red streaks, *i.e.*, the streaks unite the centres of adjoining acini (see fig. 438). By this means a remarkable design is produced which is quite irregular in relation to the lobular arrangement for it demarkates as connected islands, areas which are situated in a red network and which touch the angles of atrophic sunken places with the brighter peripheral parts of several adjacent lobules. Such a prominent area looks like one lobule at times, and the architecture of peripheral portions is not recognizable macroscopically. These small islands project more if they are rich in fat (congestion design).

The liver cells often contain abundant fat in the parts free from the atrophy, derived from digestion and brought in by the portal vein, but partly non-oxidized on account of defective gas exchange. The author, as well as Schilling, have seen fat in Kupffer's cells. In this way the atrophic, cyanotic, fatty, nutmeg liver is developed, with deeply sunken, red brown central, and light yellow peripheral parts of lobules projecting on the section surface. Cyanotic atrophy is not always equally marked everywhere; sometimes a whole lobe is favored, or dark atrophic areas in spots and streaks resemble maps. They may simulate angiomas. The outer surface may show flat furrows and indentations corresponding to the atrophic areas.

These irregularities in the degree of congestion depend, no doubt, on the irregularity of pressure in the angular ramifying branches of the hepatic vein (see Orth, Schantz).

In the second stage there is the same increase of connective tissue as in other organs under the influence of venous hyperemia. It is most marked in the dilated hepatic veins which normally have quite delicate walls and in the central veins which should appear macroscopically only as openings in the parenchyma, but now show fairly thick fibrous walls. The periportal connective tissue is also thickened at times, and appears in the form of white strands between the acini. The consistency of the liver consequently becomes tough and firm, and the surface is wrinkled (cyanotic induration; indurated atrophic congestion liver; hard nutmeg liver).

The remaining parenchyma may undergo compensatory hypertrophy (Saltykow), and light cells with clear protoplasm may appear (young liver cells, Adler), and thus on cross section, among the dark blue or brown red atrophic areas are prominent grayish yellow striae and granular groups. These may gather into large foci (fig. 431), or dendritic branchings following the ramifications of the portal vein or they surround sublobular veins in rosette form and look as if composed of enlarged acini. In time, however, these hyperplastic foci also succumb to the atrophy. In more pronounced degrees it is usually easy to demonstrate hypertrophy and hyperplasia of the reticulm fibres, (see p. 886), especially in the center of lobules (Herxheimer), (Barbacci described proliferation of these fibres as the basis of the hard arteriosclerotic liver).

When the connective tissue is abundant, a picture resembling cirrhosis may be produced. The liver is smaller, especially the right lobe, and not rarely is globular and of firm consistency; the capsule is thickened, sometimes finely fringed, with granular surface, but not regular as in true cirrhosis. But occasionally the increased connective tissue of Glisson's capsule surrounds whole groups of lobules, hence the characteristic change in structure does not occur, as in cirrhosis (Eisenmenger, Herscheimer, aus dem Bruch, Fahr). The remarkable dark brownish blue also differentiates congestive induration from typical cirrhosis. But combinations of both do occur (see below).

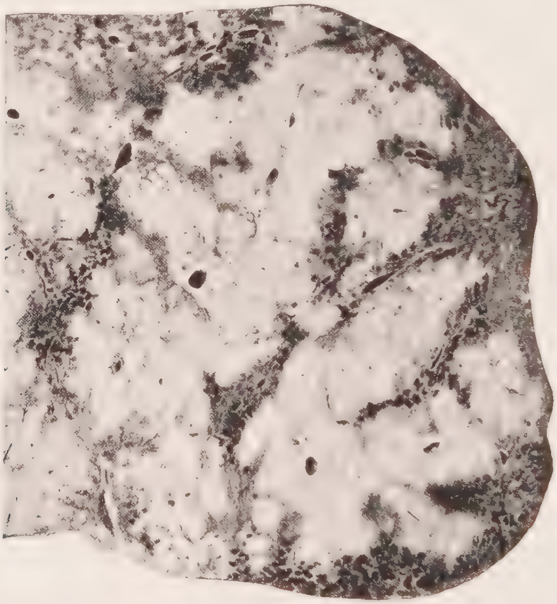


FIG. 431.—Regeneration of liver tissue in stasis liver of woman 34 years old with mitral stenosis; $\frac{3}{4}$ nat. size.

Cornil and Ranvier, (see also Geraudel, Bauer), gave the name "cardiac cirrhosis" to a connective tissue process starting in the vicinity of the sublobular veins and the central veins which separated portions of tissue (pseudo lobules). In their centers are branches of portal veins and bile ducts and the capillaries are much dilated in the peripheral parts. Piery is of the opinion that the picture is not sufficiently explained by the demonstration of prolonged stasis alone, but requires the addition of inflammatory cirrhotic processes, the progress of which are favored by venous obstruction. This general opinion, that stasis is a predisposing factor in cirrhosis, is shared by Heizheimer, Fahr, and others.

Mallory described hemmorhagic necrosis in chronic congestion of the liver, and Oertel saw central necrosis and hemorrhages combined with intralobular bile stasis and bile saturation (with icterus). For more details as to the so-called cyanotic icterus appearing in cardiac diseases and congestion liver, see Lepehne, lit.

Occlusion of branches of the hepatic veins is frequent when numerous carcinoma metastases are implanted in the liver. It is followed by hemorrhagic infiltration of the area involved and the brown red color is sharply outlined from its surroundings. The lobular design within the hemorrhagic infiltration may be preserved, in other cases, erased, and the columns of the atrophic liver cells as deep red areas sink below the section surface. This is not a true hemorrhagic infarct. Thrombophlebitis develops not only in connection with tumor nodules, but also in the vicinity of purulent foci in the liver. Independent obliterating endophlebitis of the main trunks of the hepatic vein was described by Chiari, and by O. Meyer (lit.) of the smaller branches also. The condition is probably of syphilitic origin. It is accompained by thrombosis and deep dark red color of the liver parenchyma. The end is fatal from hydrops, especially ascites (see also Huebschmann, Schmincke, Hess, lit.). According to O. Meyer, there is a close relationship to primary portal vein sclerosis which is also syphilitic in origin (see p. 894). Penkert reported congenital hepatic vein occlusion in the so-called idiopathic obstruction liver. Mechanical injuries at the insertion into the vena cava, and pulling, have been mentioned to explain this endophlebitis with thrombosis; Kretz, Umbreit and Issel speak of primary thrombosis from central circulatory disturbances (cardiac diseases). Sternberg weighs the evidence of whether thrombosis is not due perhaps to an infectious disease, especially influenza (lit. by Meystre, Hess, Reiniger).

Vanzetti believes a special form of cirrhosis is due to a productive phlebitis of the hepatic veins combined with productive phlebitis of the cava.

Retrograde embolism into the hepatic veins is remarkably rare. The emboli are thrown against the venous current by the pulse of the wave of the right auricle, a process known as venous embolism or retrograde transport (see p. 169). It is rare for abscess formation to take place in this way from infected emboli (see p. 919); lit. by Reininger.

The author saw retrograde thrombosis into the hepatic vein under the following circumstances: thrombosis of the vena cava in an 8 year old boy with multiple abdominal abscesses following appendicitis; the thrombosis continued to the lower branch of the hepatic vein coming from the right lobe; there was a congestion infarct as large as a hen's egg, angular and sharply demarcated on the liver surface. (See Theis, for alleged primary hepatic vein thrombosis.)

Simple Circulatory Disturbances in the Portal Vein and Hepatic Artery.– Occlusion of the trunk of the portal vein, sometimes suddenly, from thrombosis or tumors is, at first, without serious consequences to the liver tissue itself, but bile secretion is quickly diminished temporarily.

Occlusion of the trunk over longer periods eventually leads to atrophy of the liver tissue. See Josselin de Jong for consequences of thrombosis of the portal vein, *i.e.*, the radicles, intrahepatic or terminal, and the trunk itself; see also Kaspar in reference to the latter. Review of pathology and therapy of occlusion of the portal vein by Enderlen, Hotz and Magnus-Alsleben (lit.).

In the regions draining into the portal vein there appear, however, pronounced hyperemia, splenic tumor often very large, sometimes complete hemorrhagic infiltration of the ileum and usually ascites. The hepatic artery nourishes the parenchyma and if it is functionally perfect, its blood supply may increase in time so that functional substitution is complete. A reverse relationship does not exist.

The modus by which this is achieved was mentioned on p. 885, and is as follows: the hepatic artery through its capillary ramifications supplies the tissue of Glisson's capsule and the interlobular channels lying within it. Then the blood reaches the venules which open into the interlobular branches of the portal vein, and from there it reaches the intralobular capillaries of the lobules.

Ligation of the portal vein in the rabbit with its four liver lobes has shown that this vein is of much importance for the nutrition of the liver (see Reddingius).

L. Pick points out that in thrombosis of the trunk of the portal vein, the common hepatofugal collateral channels are essential, as far as the hemodynamic balance is concerned, but on the other hand, the "accessory" portal veins of the lesser omentum leading directly into the liver and anastomosing with the veins of the stomach wall and the duodenum, offer the possibility of a functionally serviceable hepatopetal collateral tract which can be utilized also for the gastrointestinal tract as a whole. Thrombosis of the portal vein may occur (*a*) by continuity from its branches (mesenteric, splenic, as in splenic infarction, tabes mesenterica with severe tuberculous intestinal ulceration, etc.); (*b*) in diseases of the liver, especially cirrhosis, (in which there may occur also a phlebosclerosis of the portal vein), due not only to the circulatory disturbances, but, according to Simmonds, also directly to a cirrhosis-producing toxin, possibly syphilis, tumors, etc. (see Borrmann, Buday, Askanasy, Sorrana); (*c*) by compression of a neighboring tumor or gall stones and by the infiltrated lymph nodes accompanying them; (*d*) by traumata, pulling, tears in the wall of the vein and subsequent thickening of the wall (sclerosis) (Saxer, Heller, Schmorl, Ponfick); (*c*) from anomalies of position such as pressure of the cystic duct on the portal vein passing to its right, (Hecht, lit.), or from an unusual lobulation of the liver and portal vein branching (Gruber); (*f*) from marantic causes such as congenital lues, malaria, phthisis, or from unknown causes (see Schulz and Muller, and lit. by Thorel and Lissauer).

Cavernous metamorphosis is rare (Risel, Verse, lit.). The trunk is usually occluded by organization of the thrombus. L. Pick described complete closure of the trunk of the portal vein by a cavernoma (phlebogenous angioma of the venous wall, p. 172). The author, Verse, and others, doubt the neoplastic nature of Pick's case on the basis of an observation of cavernous thrombosis in a 56 year old woman affecting the trunk and intrahepatic branches of the portal vein, with thrombosis to the splenic and several mesenteric venous branches, with hemorrhagic infarction of several loops of ileum. The case corresponds histologically to that of Verse. It is probably an old thrombosis with extensive recanalization and formation of collateral capillaries (see Emmerich, Gruber, Kaspar). Beitzke and Hart think of a congenital structural anomaly (malformation).

Chronic portal occlusion by organized thrombi or by sclerosis of the portal vein with narrowing is observed as the result of the healing of a pyelophlebitis (see Weil, lit. Gohrbandt), or independently in such primary disturbances of the liver as are due almost always to syphilis (Simmonds). It is usually accompanied by marked splenic enlargement (von der Weth, lit.). Not rarely, it proves fatal from bleeding from esophageal varices (Risel, L. Pick, lit.). See p. 917 as to pyelothrombosis in connection with pyelophlebitis.

If, however, the pressure in the hepatic artery is exceptionally low, if one of its branches is occluded, or the artery is sclerotic or has been ligated (Rattone), or there is general venous stasis, a sort of hemorrhagic infarction results from embolic or thrombotic occlusion of a branch of the portal vein whether simple or carcinomatous, or, as seen by the author, from tubercles, (so-called atrophic red infarct, Zahn). It occupies a circumscribed, approximately wedge-shaped area usually reaching to the surface, dark red in color with its apex pointing to the hilum. The blood of the hepatic vein flows back into the region cut off from the portal blood. The lobular architecture is preserved at first, the central zone is differentiated from the periphery by its dark color; on the whole, such foci do not differ from the liver of common congestion, except in the circumscribed discoloration (see Chiari). Atrophy and induration follow.

Small branches of the portal vein may be occluded without causing circulatory disturbances, because the hepatic artery acts as a collateral through the interlobular anastomoses mentioned above. But if the portal vein twigs beyond the interlobular anastomoses are occluded, or if the interlobular portal vein branches themselves are obliterated or thrombosed, *e.g.*, in cirrhosis of the liver, or tumors (carcinoma, see Pressburger), atrophy and extensive necroses result with or without hemorrhage (anemic or hemorrhagic infarct). The necrotic masses are sometimes grass green from bile pigment and may have the consistency of soft putty. The branches of the hepatic artery are often much dilated (fig. 443), but they cannot give up their blood to the lobular capillaries. When numerous branches of the portal vein are occluded within the liver, especially by cirrhosis, collateral branches (hepatofugal) take their place, but this does not always prevent congestion and ascites. The most important collaterals are between the roots of the portal vein and the inferior esophageal vein which enters the azygos, and the hemorrhoidal vein which enters the hypogastric vein (see p. 165 and under cirrhosis of liver).

In eclampsia, which usually appears toward the end of pregnancy, at the beginning of delivery, or sometimes during the first half of gestation (Eisenreich and Schmincke, lit.), fibrinous and hyalin thrombi are found in the capillaries, small interlobular arteries and branches of the portal vein, which, like the injuries (fatty degeneration and necrosis) to the capillary endothelium, are probably of toxic origin. (See Seitz, who also assumes hyperemesis gravidarum is due to a toxemia from fatty degeneration and necrosis of the liver; see Heinrichsdorff, in opposition.) The thrombosis is accompanied by focal hemorrhagic and anemic necroses of the parenchyma starting from the periphery of the lobules which produce the macroscopic changes first pointed out by Jurgens (Schmorl and others, also Konstantinowitsch, Coelen, lit. Wegelin). In typical cases, the liver surface is completely covered with red spots, or dainty, leaf-like, or map-like marblings slightly sunken here and there, but elsewhere without differences in level. The spots are frequently confluent at the insertion of the coronary ligament where the surface is diffusely red and the capsule has blood beneath it. On section, we see everywhere, irregular, angular, red spots, the architecture of lobules partly retained and partly lost with darker and deeper centres, or slightly bulging, dark red, gray, and opaque configurations (fig. 432). Isolated pale areas are rounded in shape with the lobules plain or faded but large and opaque. The author has seen livers filled with necrotic foci, angular, or map-like, yellow, sometimes edged with delicate, light yellowish white, or small red seams, dry and wedge-shaped. Some were as large as hen's eggs, within which numerous thrombosed vessels could be demonstrated microscopically, while the typical red foci were absent (see Lubarsch, Heinrichsdorff). The author has often seen typical changes in newborns suffering from spasms, born of mothers with eclampsia. When the subcapsular blood blisters rupture, the hemorrhage into the peritoneal cavity is sometimes of dangerous proportion. In addition to the liver changes, small petechial hemorrhages are frequently observed in serous and mucous membranes, kidneys, lungs, brain and its membranes (see p. 162 for large, fatal cerebral hemorrhages).

For placenta cells and fat embolism, see under lung, pp. 387 and 388.

According to Freund, the mortality of eclampsia is about 10% of which about 7% are cases in whom severe irreparable injury to the liver was sustained even before the attacks of eclampsia occurred, while in 3%, death is due to the kidneys and secondary diseases of the lungs and heart. Later investigations show that the liver may be affected to varying degrees, just as there are varying clinical forms such as (*a*) the typical with convulsions; (*b*) atypical without convulsions; (*c*) severe hyperemesis gravidarum, all with possible icterus—and various other discomforts of pregnancy such as ptyalism, neuritis, visual disturbances, etc., (see Schiekle, lit).

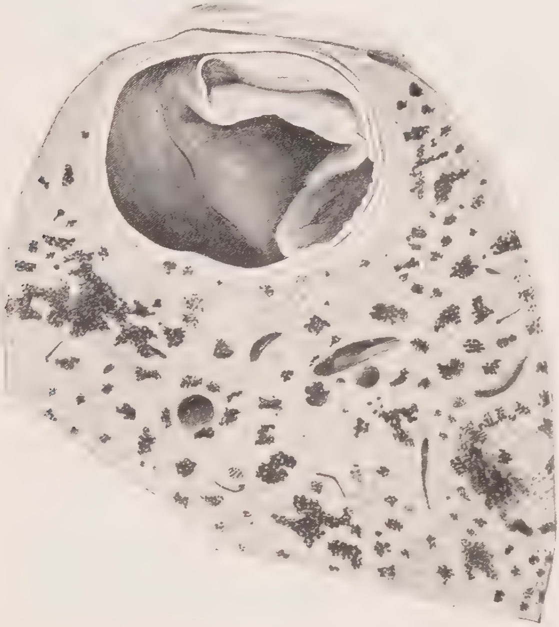


FIG. 432.—Piece of liver with many hemorrhagic foci in eclampsia. A hydatid ecchinococcus also present. The translucent animal membrane is rolled in and detached in folds. Attachment to diaphragm; woman 36 years old; ¾ nat. size.

There are many theories to account for these disturbances during pregnancy. We might mention the assumption of fetal toxic metabolic products which reach the maternal organism, since the symptoms disappear with the death of the fetus (see, *e.g.*, B. Molinari). Another theory speaks of the absence of an enzyme in the maternal blood which allows toxic catabolic products of large molecular composition to appear derived from chorion cell products which cause a toxicosis showing sometimes as eclampsia, sometimes as hyperemesis, or as changes in the liver, or psychoses, nephroses, etc. (R. Freund). Some mention placental toxins in the maternal blood which cause coagulation and injury to cells with nephritis; others suppose there is overloading with protein bodies, especially globulins of an acid nature in excess of the available alkalies which should keep them in solution. Thus the viscosity of the blood is changed, the current is slowed and capillary congestion leads to stimulation of the vaso-motor centre. This in turn causes contraction of vessels in the skin and musculature and dilatation of those in the internal organs; multiple capillary thrombi appear in these organs, and finally carbon dioxide accumulates, causing asphyxia and death. None of these numerous theories has stood a rigid test (comp. v. Miltner). For lit. in reference to eclampsia, especially the recent theories, see appendix.

The Hepatic Artery.—Experimental occlusion of the healthy hepatic artery which arises adjacent to the right gastric artery (v. Haberer. lit, Narath) is followed by fatal, complete anemic necrosis of the liver (see Budde for variations of the hepatic artery). But Narath was able to prevent anemic necrosis after ligation of the hepatic artery by an arteriovenous anastomosis of the portal vein and an adjacent artery or the hepatic artery itself. That the hepatic artery is not merely a vessel supplying nutrition, but is also of functional importance, is proved by the fact that after the establishment of an Eck fistula, (anastomosis between portal vein and vena cava), the liver can carry on its functions (see Perroncito, and esp. Enderlen, Hotz and Magnus-Alsleben).

If the hepatic artery is markedly sclerotic and narrowed, the effect is likely to be absent, because sufficient collaterals were previously opened. The anastomoses of the arterial branches thus prevent consequences from occlusion of single ones. Only when minute branches are occluded, *e.g.*, by emboli from endocarditis, or when there is cardiac failure, does focal hemorrhagic infiltration take place. It is usually followed by anemic necrosis and is hardly recognizable externally; on cross section of the liver the area appears as a map-like, cloudy, clay-colored anemic infarct often with a light yellow rim (see illustr. by Kretz).

Occlusion of a large branch of the hepatic artery sometimes causes necrosis possibly followed by fibrous cicatricial change in a larger area of the liver. The author saw it in a 42 year old man following trauma (kick of a horse 8 months previous). An aneurysm almost as large as a walnut developed in a large intrahepatic branch of the artery, perforated into the hepatic duct, and caused death by hemorrhage into the duodenum (publ. by Mester).

Aneurysms of the hepatic artery are rare; besides a traumatic origin, infection as a cause must be considered. Death occurs chiefly from rupture, occasionally, as in the cases of Waetzold and Reichmann, simultaneously with rupture of the liver (lit. in appendix).

Extensive anemic necrosis (anemic infarcts) is sometimes found in livers containing many carcinomatous metastases, and in deep, penetrating, traumatic rupture of the organ (lit. by Chiari), with tearing (Orth), and vessel thrombosis (branches of the portal vein or hepatic artery, the author). These sequestrae may develop days after, or immediately following severe trauma because of separation, fragmentation, or from plain direct necrosis of liver tissue. Healing by organization has been reported; see Wakasugi: necrosis after stab wounds; lit. in ref. to trauma of the liver by Boljarski, Finsterer, Dietrick, Gruber. See Walz and Holle for mechanism of the cause of rupture of the liver by blunt force. For literature on central ruptures with tears and closed cavities mostly filled with blood and usually followed by hepatic abscess, see Bauer.

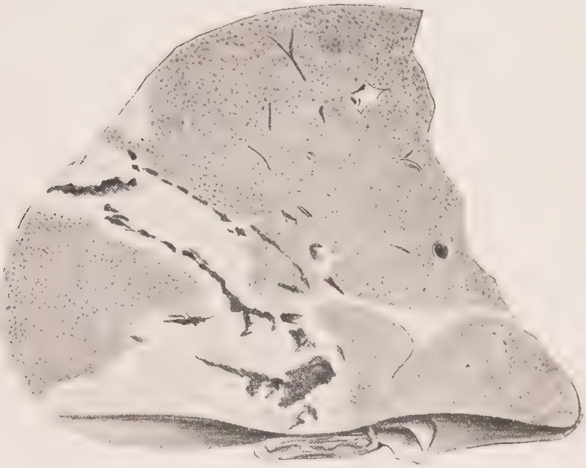


FIG. 433.—Rupture of liver with wedge-shaped anemic necrosis. Piece of horizontal section of right lobe. Below, the sanguinonecrotic right adrenal alongside the vena cava. Man 24 years old run over by wagon; ½ nat. size.

Anemic infarcts *i.e.*, necroses are known to occur in nodular periarteritis, (p. 121).

Hemorrhages.—Apart from the cases mentioned—occlusion of the hepatic vein, eclampsia and trauma—hemorrhages into the liver are due to changes in the vessel walls, the hemorrhagic diatheses (purpura, etc.), various infections, (syphilis, see Devic and Beriel), and intoxications, especially poisoning by phosphorus, etc. They are mainly multiple, subcapsular, and of small extent. But in a newborn, Bonnaire and Durante described exsanguination into the abdominal cavity from the rupture of immense blister-like subcapsular hematomas of the liver due presumably to the influence of a maternal intoxication or infection (see them for details and good illustrations, also Ludwig lit.). Meyer described an unusual form of globular miliary hemorrhages, the demonstrated cause being an acute, perhaps agonal, tearing of dilated hepatic veins, in pulmonary tuberculosis. Schonlank thinks that the blood foci are due to a toxic ferment thrombosis. Mittasch believes a toxic noxa causes focal injuries to the cells (necrosis), and capillaries, (dilatation and thrombosis). He never saw rupture. Small veins may also be dilated. Coughing favors angioectasia. The foci may eventually undergo connective tissue organization (see Peltason).

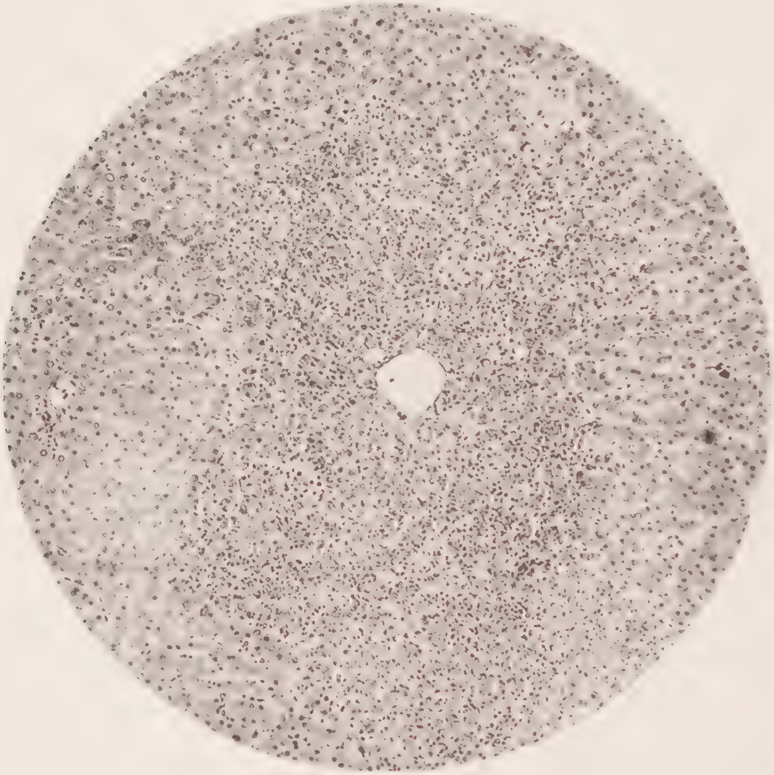


FIG. 434.—Focal necrosis of the liver in sepsis. × 110.

Edema.—Edema is principally localized in the periportal connective tissue which become thick gelatinous strands. According to Birch-Hirschfeld, the spaces between the liver cell scaffolding and capillaries (perivascular lymph spaces) can be distended by serous contents so that the liver as a whole is larger and soggy. But macroscopic diagnosis is uncertain. Edema may be mechanical obstructive, as in cardiac lesions, or develop after birth; it may be inflammatory from the bile channels, portal vein phlebitis, etc. Birch-Hirschfeld thought that edema compressing the bile ducts may give rise to icterus in the newborn. This has never been seen by the author. In adults we know that edema, however excessive, never alone causes icterus.

Simple and Brown Atrophy of the Liver

Pressure atrophy from outside influences has been discussed, also cyanotic atrophy from venous congestion and the atrophy due to local disturbances of nutrition. We shall encounter other hepatic conditions which cause atrophy from pressure such as the constriction of proliferating connective tissue, pressure from tumors or parasites. The acute yellow and red degenerative atrophy are in a class of their own (p. 907).

In simple and brown atrophy, the liver may retain its normal light brown color or become darker; the organ as a whole is considerably smaller, perhaps reduced one-third of its normal size, due to loss of volume of the cells, especially those in the centre of the lobules. They become small, rounded or angular, cloudy, some disappearing entirely. In brown atrophy, the cells are pigmented by angular or rounded yellow or brown granules (fig. 436), but it must be remembered, that liver cells physiologically are of a diffuse brownish yellow color. The central parts of the lobules are more highly pigmented.

The loss of weight may be enormous indeed, as is shown in a 73 year old woman whose liver weighed 542 gms. (collection of Basel).

Simple atrophy is seen best in starvation if death has occurred in a comparatively short time. Brown atrophy is met chiefly in inanitions of longer duration, *e.g.*, in esophageal carcinoma, and the general atrophy of age. In both forms, the surface of the liver is smooth, or finely wrinkled, since Glisson's capsule is too large. The relative increase of connective tissue makes the consistency firm, often leathery. The section surface shows very distinct, delicate lobular architecture, but the lobules are remarkably small, their centers dark brown and at a somewhat lower level. The peripheries are light brown to yellowish brown. The microscopic picture is clear and orientation quite easy, in fact, in no other liver can so many clearly differentiated lobules be seen in one microscopic field as in brown atrophy.

The margins of the liver are the first to atrophy; they become sharp, flat, white, fibrous, and sharply outlined from the rest of the parenchyma. The liver substance disappears completely in this ragged, translucent fibrous edge and only occasional white strands are visible corresponding to vessels and larger bile channels lying in a fibrous, almost nonvascular, tissue.

The brown discoloration is due partly to the retention of pigment by the cells which can not change it into bile pigment, and partly to an autochthonous granular pigment formed with the progressive reduction of cells. The pigment contains no iron. See Brahn and Schmidtmann in reference to its composition.

Fat Infiltration of the Liver—Fatty Liver—Lipomatosis of the Liver

Fat infiltration is exceedingly common. The cells, especially in the peripheral parts of the lobules, contain fat in granules and droplets (fig. 435). The protoplasm is unchanged and not cloudy.

When much fat is present, the nucleus is forced to one side and by the union of numerous droplets, a large, darkly outlined fat globule takes the place of the protoplasm. When the globule is very large, the cell as a whole is increased in size (fig. 436). In marked fat infiltration, sufficient pressure may be exerted on the liver cells and capillaries to interefere with their function.

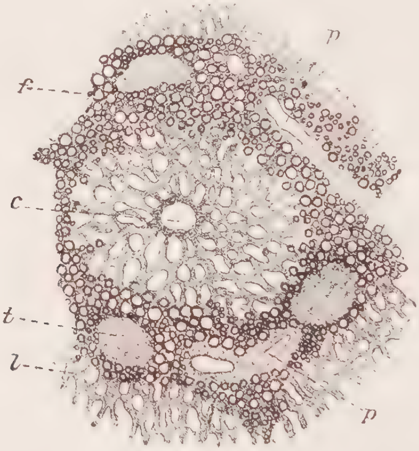


FIG. 435.—Fat infiltration of liver in a phthisic; the fat (f) lies in the peripheral parts of the lobules. c, central vein distended; brown pigment in surrounding liver cells; p, branches of portal vein; l, columns of liver cells; t, miliary tubercle in interacinar tissue; a second above, a third to the left. (Low power.)

Macroscopically, the liver is voluminous, its weight is doubled or more, the parenchyma fills the tensely stretched capsule and the edges are rounded; the consistency is doughy and non-elastic, finger marks disappear slowly or not at all; the tissues are fragile, and the fatty liver has a tendency to rupture. The author saw fatal abdominal hemorrhage due to multiple ruptures of the liver without external injury, caused by falling out of bed in delirium tremens.

The specific gravity diminishes, the organ may even float. The color is pale, brown yellow, butter yellow, or in anemia, clay colored. If it is hyperemic also, the color is yellowish red, and with decomposition, quite red (cloudy pale red). On sectioning, the knife is coated with fat, and a thick creamy juice containing fat globules can be squeezed from the section surface.

In moderate degrees the lobular architecture is quite evident, the peripheral zones are fat-laden and yellow. They appear as a dainty projecting network which encloses the darker central zones lying deeper and sharply demarkated. In extreme degrees, the liver looks like pate' de foie gras; the lobulation is indistinct since the central zones are also filled with fat and since the lobules are forced together and the interlobular boundaries with their vein branches are almost completely obscured.

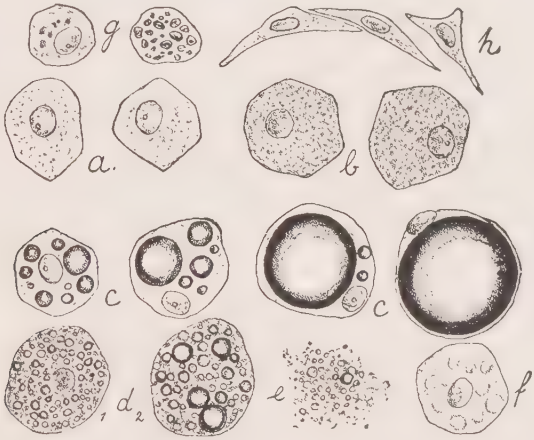


Fig. 436.—A 2, normal liver cells (unstained); b, cloudy swelling in acute sepsis; c, fat infiltration, various degrees; d, fatty degeneration, 1 finely granular in sepsis, two liver cells with large granular fat in phosphorus poisoning; e, excessive fatty necrotic disintegration; f, glycogen infiltration in diabetes; g, atrophic liver cells, one with little, the other with much pigment; h, flat atrophic liver cells (about × 500).

If passive congestion is also present, the central zones of the fatty nutmeg liver are still more depressed, dark brown red in color and diffuse one into the other. The yellow peripheral rings (part of the network) stand out on the section surface, but are frequently broken. The arrangement of the fat infiltrated parts in some cases is in the form of prominent spots, or islands composed of the peripheral zones of neighboring lobules. This granular fatty liver slightly resembles cirrhosis. It may be developed by emaciation of a homogeneous fatty liver. See Helly and W. Fischer as to different types of localization of fat in the liver.

Focal fat infiltration may be due to embolic or infectious-toxic processes.

The angular anemic spots described on p. 888, must not be mistaken for fat infiltration.

Under what conditions does fat infiltration of the liver occur?

In mild degree it may be physiological, due to fat consumption. During the period of digestion, fat is found in the peripheral zones being brought there by the portal vein. During pregnancy and lactation the liver contains more fat. Two to 3% is undoubtedly normal, and it is difficult to say when fat infiltration becomes pathological. Infiltration appears in apparently contrary conditions, *i.e.*, overnutrition, and atrophy.

In Overnutrition.—It is found among individuals who consume foods rich in protein, fat, and especially carbohydrates, which in excessive quantities produce fat. It is marked with excessive starch intake combined with little exercise (as in the geese raised for paté de foie gras). In some individuals there appears to be a special disposition to lipomatosis, and general obesity, with accumulation of fat in the subcutaneous tissues, muscles and mesenteries. But it must be emphasized that obesity is by no means constantly accompanied by pronounced fatty liver. We see fatty livers in drinkers, especially beer drinkers, since they consume a high percentage of carbohydrates, as well as alcohol. Alcohol diminishes the oxidation of fat; since it is quickly burnt up, it protects fat. A fatty liver may be present for years. In drinkers, it may eventually be continued with cirrhosis.

In Atrophy.—In contradistinction to these conditions, fatty liver appears quite frequently in individuals emaciated by long illnesses, or suffering from cachexia, anemia, or pulmonary phthisis, in whom the fat disappears from other parts of the body. Since the number of red blood corpuscles is decreased, it was thought that the oxidation of fat was therefore diminished. Fat storage in the liver may also be due to the quick disintegration of albuminates, which takes place in these marantic conditions and in chronic cachexias, or it might be possible that fat is displaced from the subcutaneous tissues, the main storage depot, and is carried to the liver, where it lies unoxidized. Congestion of the hepatic vein, especially frequent in phthisis, prevents active diffusion between blood and liver cells, thus doubtless allowing the fat to remain in the cells.

Many things formerly interpreted as fatty degeneration, due to a metamorphosis of cell albumen into fat, are in reality fat infiltration. (Fibiger and Herxheimer give a good resumé of this question.) This is true particularly in experimental phosphorus and phlorizin poisonings in which Lebedeff, Rosenfeld, (see also Schwalbe, Wuttig) claim they demonstrated a migration of fat from the fat depots and alimentary tract to the liver by way of the blood, but it is questionable whether different melting points alone suffice to characterize the different kinds of fat. In degenerative fat infiltration, (see p. 52), in contradistinction to simple fat infiltration, it may indeed be assumed, and in some cases can be proved, that the protoplasm of the cell itself is diseased. Some call both fatty degeneration (lit. by Helly, see p. 907).

Fat in Kupffer's star cells is frequent, but the quantity does not run parallel to that in the liver cells (Schilling, W. Fischer). In diabetes, the fat content of the star cells is so pronounced that it gives a very characteristic picture (Rossle). In one case, Kawamura found a doubly refracting fat (cholesterin-ester degeneration).

It is only when pathological fat formation is confined to a small area that it is a question of metamorphosis of protoplasmic substances into free lipoid bodies in which the visibility of the lipoids is involved, or in which swelling and separation of finely distributed lipoid granules in the protoplasm occur, *i.e.*, especially in autolysis (adipocere) (Aschoff).

Simple and Inflammatory Degeneration (Parenchymatous Hepatitis)

Albuminous Clouding and Fatty Degeneration of Liver Cells.—Fatty degeneration is an entirely different process from fat infiltration. While in fat infiltration, the fat is merely added to the otherwise healthy cell, in fatty degeneration, the protoplasm itself is severely damaged and shows all the signs of albuminous and fatty disintegration. These processes are usually evenly distributed throughout the entire liver.

In cloudy swelling, (first stage of parenchymatous hepatitis), the liver cells enlarge, swell, probably through absorption of water; the protoplasm becomes granular, cloudy, even the nucleus may become indistinct (fig. 436). On the addition of acetic acid, this albuminous clouding disappears. The liver is more or less enlarged, soft, even mushy, opaque and dull gray, appearing as though "boiled." It is paler and contains less blood than normal which is perhaps due to pressure of the swollen cells on the capillaries. The lobules are enlarged. Cloudy swelling may regress or progress to fatty degeneration.

In fatty degeneration, (the second stage of parenchymatous hepatitis), the cells, somewhat enlarged and swollen, can still be seen quite plainly with the microscope; their contents are light, refracting fat droplets (fig. 436), and cloudy protoplasm; the droplets vary in size, in some diseases such as acute phosphorus and toad stool poisonings, they are especially numerous and large, in other cases they are small, almost like dust. The presence of larger fat droplets often makes it difficult to differentiate from fat infiltration. In the most severe cases, the cells disintegrate into a debris of fat and protein granules which can be seen quite well in smear preparations. The nuclei break up by karyorehexis and chromatolysis. Slight degrees of fatty degeneration may clear up, and liver cells, completely destroyed, may be replaced by regenerative proliferation.

Macroscopically the diffuse fatty degenerated liver is large at first, becoming small later; it is flaccid, soft, the section surface is cloudy, it lacks distinct lobular markings, and is yellow red, yellow gray or yellow. If anemia is also present, it is clay colored. If icterus is likewise present, the dark, golden yellow, saffron liver is produced, such as is seen in acute atrophy, and at times in severe cases of typhoid fever, cholera, and small-pox. The patients die of cholemia, (see cholemia, p. 1009).

Etiology of Fatty Degenerattion and Cloudy Swelling.—Fatty degeneration or degenerative fat infiltration is seen as one of the results of infectious, toxic, and simple degenerative processes. In both instances, a hematogenous injury to the cell protoplasm is essential to this pathological infiltration.

Infectious-toxic fatty degeneration probably does not develop directly, but is preceded by cloudy swelling (parenchymatous hepatitis). These changes are met in severe infections such as pyemia, sepsis, typhoid fever, recurrent fever, variola, erysipelas, etc., (see Hildebrand). The fat granules are frequently extraordinarily minute (fig. 436). Kupffer's cells, which may be increased in number, also contain fat droplets (v. Platen, Asch, G. Koch) just as in the blood diseases and poisonings, presently to be discussed. We assume there is an injury to the star cells, *i.e.*, a degenerative fatty infiltration (Schilling, lit.). For cholesterin-ester infiltration (cholesterin steatosis) of star cells in diabetes, see Kawamura.

Simple fatty degeneration is seen in chlorosis, after hemorrhages and in pernicious anemia. In the latter, the organ is diminished in size; on section, the central zones are involved, and sulphur yellow spots, not raised, are seen in regular arrangement corresponding to the centres of lobules; otherwise the section surface is light brown in color from infiltration of blood pigment. As Rossle emphasizes, this central fatty degeneration of pernicious anemia is also found in anemias due to other causes such as syphilis, sepsis, tumor cachexia, advanced age, chronic intestinal catarrh, etc., and may be combined with congestion. In acute phosphorus poisoning, and to a less degree in arsenical poisoning, (see Eichhorst), diffuse fatty degeneration is found. Often the fat globules are large as those in simple infiltration (fig. 436). In poisoning by antimony, prussic acid, chloroform (prolonged action), iodoform, chloral, carbon monoxide, and alcohol, cloudy swelling and fatty degeneration set in, although the latter never reaches the high degree as in phosphorus poisoning. Fatty degeneration is usually found also in the kidneys, heart muscle and vascular endothelium. It is accompanied by hemorrhages, (chiefly in the liver), in toad stool poisoning, in which acute cell destruction is combined (hemorrhagic fatty liver, see M. B. Schmidt, Herzog, lit. Eug. Fraenkel, Treupel, Rehorn, clinical and lit., see p. 910). After prolonged and repeated inhalations of chloroform, necroses appear in the central zones and the periphery shows marked fatty degeneration (Bock, lit.); fatty degeneration of the heart muscle, epithelium of the renal cortex, intima of the aorta, (see there), etc., are also observed. General fatty degeneration of the liver occurs in cases of periodical vomiting with acetonemia (Moser, lit.), and in experimental feeding of the precursors of acetone (butyric acid, etc., lit. Moser). Partial fatty degeneration is caused by nutritional disturbances in vessel lesions.

Other Differences between Simple Fat Infiltration and Fatty Degeneration.—The difference is recognizable by the size and consistency of the liver. In simple infiltration both increase; in degeneration, the liver is also enlarged in the beginning but it is soon reduced in size, the consistency becomes steadily softer, it is cloudy on section, and without lobular etchings. If the fat is removed by alcohol, ether, etc. from a section, the infiltrated liver still shows a connected system of cells perforated by vacuoles, which were filled with fat. With the same technique in fatty degeneration, (10 to 14 days after phosphorus poisoning, or liver of red atrophy, etc.), there is an extensive disintegration of cells with disappearance of architectural design.

Acute Yellow and Red (True) Atrophy of the Liver

In this extremely pernicious disease, with no uniform etiology but chiefly infectious-toxic in origin, a rapid atrophy of the liver occurs in the acute form in one, and in the subacute form in three weeks. Sometimes it is plainly recognizable clinically and is due to granular and fatty degeneration.

Macroscopic Conditions.—In acute cases, the liver is more or less reduced in size; exceptionally, it is enlarged. The organ is flabby, wilted, can be folded, friable, almost semi-liquid. The edges are sharp and flat, the capsule is wrinkled; larger or smaller yellow or grayish red areas are elevated above the surface. The section surface is diffuse yellow, or if the usual icterus is present, ochre yellow like moistened dried rhubarb. An opaque liquid pulp can be scraped from the surface. In subacute cases (the more frequent, according to Seyfarth), it is marbled red and yellow, with the red parts appearing denser, firmer, and tougher (Waldeyer) and sometimes penetrated with fine gray trabeculae like a spleen (Glisson's capsule, see below). The yellow parts bulge like cushions; the organ as a whole is tough elastic to the touch. The deep red color of hemorrhage is seen around the larger branches of the portal vein as well as in the yellow and red areas. The lobular design is usually almost completely effaced, but may still be visible in the yellow spaces, which are usually swollen in the earlier stages. In the red foci it may not be gone completely, but can be recognized by a network from the remaining Glisson's sheath shrunken by the disappearance of the liver cells, but still outlining the lobular boundaries (see Verse). Given sufficient time, red atrophy is the next stage following yellow atrophy and Zenker speaks of a transition of fatty into hyperemic atrophy. The color is due to filling of the dilated capillaries between which the columns of liver cells have disappeared with the exception of some granular remnants. Of the lobules only the capillary scaffolding remains. The disintegrated liver parenchyma is removed, mostly by way of the lymphatics and the bile channels.

The liver may diminish to one-half or one-third its size and its weight may fall to 750 gms. or less. All dimensions, especially the thickness, decrease. The organ is flattened.

In relatively old cases, red to brown red is the predominant color and only a few yellow islands are seen. The bile channels and the gall bladder contain but little bile and that is light in color, transparent, or slightly cloudy.

The entire liver is not always involved in this degeneration, and the left lobe is usually more severely damaged than the right. The author saw the lower part of the right lobe preserved with only moderate congestion and peripheral fat infiltration. It is impossible, as recently emphasized by Eug. Fraenkel, to construct a conception of acute atrophy which satisfies all cases.

If such a liver is left exposed to the air, especially in hot weather, a white, membranous, mold-like coating forms on the section surfaces and walls of vessels, firmly attached and somewhat rough to the touch; it consists of crystallized leucin (amido capronic acid) in rounded deposits, and tyrosin (oxyphenylamidopropionic acid) in sheaves. These decomposition products of protein bodies are found not only in acute atrophy of the liver but also, although not so abundant and regular, in septic-infections, and phosphorus poisoning.

Eug. Fraenkel by excising bits of liver, disproved Umber's statement that the soft cadaveric liver of acute atrophy is due to post mortem changes. But it is not astonishing that occasionally relatively few destructive signs are encountered in these excised pieces, especially if taken in an early stage (Hauser). It is evident that some autolytic change must take place post mortem, and to a certain extent, it contributes to the aspect of the liver (see Hauser).

The kidneys, the heart and muscles also show fatty degeneration, but rarely pronounced. The spleen is usually swollen, and liquefying.

Microscopically where the lobular design is still plain, we see hydropic swelling, albuminous clouding and fatty disintegration of the liver cells both in the peripheral and central zones. Isolated, cloudy, fatty, granular cells and cell remains can be seen in the ochre yellow areas. Between the wide capillary network are small cells of an icteric color, most of them necrotic, with fatty granular protoplasm and non-staining nuclei.

In the red areas, the cells can hardly be recognized, but the capillaries are well filled and between the wide meshes of their network which can be sharply outlined by special stains (see Huzella), is detritus consisting of fat and protein granules and granular or crystallized bile pigment. An active cellular proliferation of the periportal connective tissue is established in which peculiar epithelial cell columns attract attention. The latter are more numerous in the periphery and correspond to the bile channel proliferations seen in cirrhosis. But the canaliculi are plumper, their epithelium is larger and they are also seen in relation to intralobular bile channels. An interesting reconstruction by Milne gives a good idea of their massive character. Solid cell strands resembling columns of liver cells are also seen; they are remains, or if no degenerative changes are present, are probably newly formed liver cells. Bile duct proliferations are often seen passing into liver cell columns, *i.e.*, joining them. Kimura demonstrated many mitoses in liver cells. This regenerative new forma-

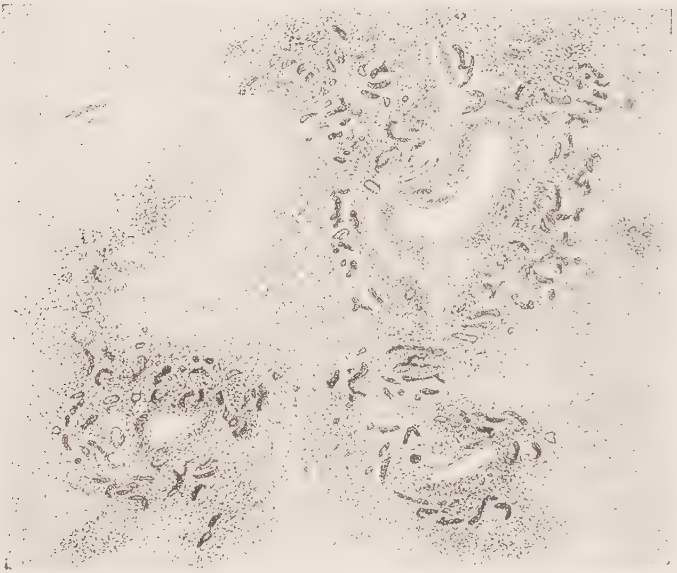


FIG. 437.—Acute yellow atrophy of liver. Three larger branches of the portal vein surrounded by the markedly infiltrated capsule of Glisson in which are numerous bile ducts and bile duct proliferations as convoluted cords and tubes; adjoining are liver cell columns; between these three chief centers of growth the liver parenchyma partly necrotic, partly atrophied, replaced by proliferating and infiltrated fibrous tissue; 4th week of disease. (Low power.)

tion is seen chiefly in the vicinity of the larger bile channels, penetrating from the periphery into the interior of the lobules. Sometimes masses of round cells are found between the bile channel proliferations in the periportal connective tissue and here and there in the neighborhood of the lobular capillaries. Hemorrhages are also seen (see fig. 437).

Transition of bile channel proliferations into liver cell columns is seen in toad stool poisoning (especially with amanita phalloides), in which there is always an accompanying fatty degeneration. There is severe, acute, destruction of liver cells, beginning in the central zones of the acini, and varying in intensity (see Paltauf, M. B. Schmidt, Herzog, Prym, etc., p. 911).

If patients recover from acute atrophy of the liver, regeneration takes place from both the remaining liver parenchyma and the epithelium of the newly formed interacinar bile channels. The picture then presented is of a more or less roughly nodular cirrhosis, or a multiple nodular hyperplasia (Marchand). On cross section are soft bulging nodules up to the size of a small apple, sharply circumscribed, of white yellow, yellow, or grayish red color, between which are gray, gray red or dark red (more or less vascularity) connective tissue strands of various widths. The surface is roughly granular, or smooth and nodular. Seyfarth (lit.) considers the nodular hyperplasia a subchronic state, *i.e.*, cases which die from the beginning of the fourth week to the seventh or eighth month after the beginning of the disease and which are accompanied by ascites. He calls such cases chronic in which the acute destruction proceeds very slowly with increasing regenerative processes added. After complete healing of the degenerative process, the picture is that of a rough lobular cirrhosis developing sometimes only after a longer period of time.

Whether the remains of the liver parenchyma or the bile channel proliferations are of greater importance in this process of regeneration is still a disputed point. Meder and Marchland thought that bile channel proliferations were the more significant. Hess (lit.) is of the opinion that the liver cells are valuable to the extent that without them, complete regeneration with nodular hyperplasia is impossible, while on the other hand, a transition of bile duct proliferation into liver cell columns occurs only if the ducts are not combined organically with the more or less typically arranged liver cells which still remain. Klotz believes the regeneration of liver tissue in nodular hyperplasia is from the bile ducts, while Herxheimer and Gerlach consider the new formation of liver cells the most important, if not the only mode of regeneration (older lit. by Schoppler).

In some cases of nodular hyperplasia, a subacute hepatic atrophy may progress with little or no regenerative processes as in the case of Jores.

Then no connective tissue proliferation may occur (see also Klopstock, Meyer).

Etiology.—Women are more often victims, especially during pregnancy and the puerperium. Juveniles are rarely attacked (lit. by Klopstock, Wegerle) and may have had only a slight illness before or, as the author saw in a 3 year old boy, they may have been in perfect health. While it is a primary disease, the process may also be secondary to known infectious diseases such as variola, erysipelas, osteomyelitis (Meder), perhaps typhoid fever, especially puerperal and other purulent and septic diseases such as peritonitis, appendicitis, etc. (Babes, Harbitz, Amberger.) Syphilis (Engel-Reimers) in the secondary stage has been repeatedly accused (lit. by Veszpremi and Kanitz, W. Fischer Graef, comp. Riess), and the rôle of arsenicals has been widely discussed. After salvarsan injections, according to some authors, there may be seen, central hemorrhagic necrosis and the picture of acute or subacute atrophy (Severin and Heinrichsdorff, Silvergleit and Foekler, Herzog and others). But besides liver tissue necrosis and bile channel proliferation as in acute atrophy, there is an enlargement of the entire organ (Sternberg). The possibility of injury by salvarsan must surely be admitted, although Herxheimer and Gerlach deny that it causes acute atrophy, and Umber reports cases in which with proved lues, the immediate resort to salvarsan checked the toxic parenchymatous disintegration.

Endogenous bacterial intoxications from the bowel (intestinal ptomains) have been considered, and the author saw acute yellow atrophy after weeks of fecal retention from stenosis of the lower part of the colon. Umber thinks that an enterogenous cholangitis is the deciding factor, favored by poor nutrition and the consequent intestinal upset. This would also explain the fact, as proved in many ways, that there is an increase of such cases. He emphasizes the constant finding of bile thrombi. Verse does not grant the cholangitic process this importance, while Eppinger, on the other hand, believes in a relationship between catarrhal icterus and acute atrophy. Acute atrophy has also been observed following chloroform anesthesia (Guleke, v. Brackel, Balkhausen), and in toad stool poisoning, (M. B. Schmidt, and lit. p. 910). In the latter, Eug. Fraenkel believes that the severe changes in the cross striated musculature consisting of destruction of the contractile substance and formation of muscle cell tubules are significant in relation to differential diagnosis. Miller believes the marked fatty degeneration constitutes a difference from the liver of true acute atrophy. The frequently observed cases of acute atrophy in individuals working in munition factories are ascribed to toxic substances (comp. gall bladder pathology). At any rate, although the etiology is not uniform, it can be said that infectious agents (spirochete) and (autolytic) toxins are the chief factors (see lit. by Quincke, Reichmann Weigett). See p. 1019 in reference to conditions similar to acute atrophy, *i.e.*, identical findings in spirochetal diseases (infectious icterus or Weil's disease and yellow fever, p. 1019). According to some authors, phosphorus poisoning also may produce the picture of acute yellow atrophy (in opposition, p. 913). The disease may be masked as icterus gravis when the atrophy is far advanced and is fatal (see icterus syphiliticus precox and acute atrophy by Michael, lit.).

Atrophy as a primary disease shows icterus in the first stage. In the second stage, severe cerebral disturbances such as coma and convulsions appear, with hemorrhages into various organs (intestines, stomach, genitalia). The pulse is much accelerated, the temperature usually normal. A post mortem temperature increase up to 42°, has been observed. In pregnant women, abortion or premature delivery usually occurs.

Leucin and tyrosin are found during life in the urine and blood. The urine usually has a low urea content. The cerebral disturbances and the hemorrhagic diatheses are thought to be due to this urea retention. The icterus is probably of hemo-hepatogenous origin.

The Liver in Acute Phosphorus Poisoning.—For experiments concerning phosphorus liver, see p. 906 and Oppel, Harnack, Manwaring. The liver may undergo such a high degree of fatty degeneration as to simulate acute yellow atrophy, but when death results in the very first days of poisoning (yellow phosphorus), every characteristic finding may be absent (fatty degeneration); in three days, however, it is usually recognizable. The liver is enlarged, its edges rounded, the color grayish yellow or yellow, and it has the doughy consistency of a fatty liver. Icterus is often present, thus giving the organ a saffron yellow color. The cells are microscopically enlarged, cloudy and filled with large fat droplets which are said to have been carried in (see p. 906) (fig. 436). Nevertheless the fat droplets are not as large as in simple fat infiltration, but, as a rule, larger than in acute atrophy. In pregnant animals poisoned by phosphorus, the fetal liver also reacts by fatty degeneration (Schwalbe and Mucke). In rare cases, death occurs late (10 to 14 days), and then many of the liver cells are completely disintegrated (fig. 436); cellular and nuclear debris is seen, some of which has been removed by absorption just as in acute atrophy. The liver is smaller, but tougher than at the beginning, the color is spotted and marbled in yellow and red, or is diffuse red. Microscopically, bile channel proliferation is found (Dinkler).

Other organic changes in phosphorus poisoning are shown in fatty degeneration of the heart, pancreas, kidneys, gastric glands, intestinal musculature, vessels and especially the musculature of the trunk plainly seen in the dirty yellow red, cloudy pectoralis. Hemorrhages are found, particularly in the panniculus adiposus (see chapter, icterus p. 1012 under phosphorus poisoning).

The differential diagnosis between phosphorus liver and acute yellow atrophy is fairly clear. In the former, fatty degeneration predominates microscopically, while in the latter, it is cell necrosis. In the former, the fat droplets are larger as a rule because immigration of fat from the fat depots takes place. The disintegration begins in the periphery, while in acute atrophy it commences in the central zones. Leucocytic infiltration and bile channel proliferations appear much earlier in the poisoning than in atrophy (comp. Paltauf). Although there are swelling and enlargement of the liver, *i.e.*, practically an acute yellow hypertrophy in the beginning of atrophy, it is a transient phase and when the cases arrive at autopsy the organ, as a rule, is much reduced in size. Conversely, the liver of acute phosphorus poisoning is usually seen at the stage when it is still enlarged because death occurs early. According to some authors (p. 905), the fat in the liver is an infiltration, but the name "fatty degeneration" seems justified because of the severe destructive processes in the cells possibly due to an autolytic ferment acting on the liver cells through the blood. In chronic phosphorus poisoning as Wegner has shown, a diffuse interstitial hepatitis leads to induration, and Paltauf believes that, especially in children, coarsely nodular hyperplasias may result similar to those sometimes encountered after acute atrophy.

In phosphorus liver, as in every severe parenchymatous degeneration, post mortem precipitation of leucin and tyrosin crystals takes place on section surfaces and vessel walls. These substances appear but rarely in the urine in large quantity.

According to Prym, the picture of toadstool poisoning (see p. 911) resembles that of phosphorus poisoning combined with acute atrophy. Autopsy findings in poisoning with amanita phalloides presented to Eug. Fraenkel a picture similar to acute phosphorus poisoning, *i.e.*, fatty degeneration of the parenchymatous organs and scattered hemorrhages. The general musculature was also severely damaged.

Interstitial Inflammation of the Liver

Several kinds of inflammations of the liver can be distinguished:

(*a*) parenchymatous hepatitis marked by cloudy swelling or by fatty degeneration, as discussed p. 905.

(*b*) purulent inflammation, abscess formation.

(*c*) chronic fibrous hepatitis.

(*b*) and (*c*) are interstitial inflammations.

Suppuration and Abscess Formation in the Liver.— Abscesses develop from the invasion of pyogenic organisms. The paths of ingress are, apart from infected traumata, the bile, blood, and lymph channels. Pyemic or metastatic abscesses are produced by hematogenous introduction of pyogenic organisms from some focus of infection via the portal vein and the hepatic artery, but most liver abscesses occur by way of the portal vein and bile ducts. In the latter, the organisms are usually colon bacilli while hematogenous invaders are chiefly pyogenic cocci (see Davidsohn) (amebic abscesses, p. 915).

1. Purulent hepatitis is initiated by the portal vein into which pyogenic organisms are introduced from its branches which may drain intestinal ulcerations, rectal, appendiceal abscesses, etc. When pyogenic organisms, usually in thrombotic material, reach the portal vein from the intestinal veins, they lodge in the liver.

The small interlobular portal vein branches as well as the intralobular capillaries are occluded, the bacteria increase in number, secondary thrombosis spreads and with the assistance of direct chemical action produce necrosis of the surrounding tissue. The liver cells are cloudy, gray, or grayish yellow, take no stain, and disintegrate. An active purulent exudative inflammation surrounds the necrotic area. The purulent exudate mixes with the necrotic tissue detritus and the mass gradually dissolves and liquefies.

Thus abscesses are formed, greenish yellow foci of pus. They may be solitary or multiple; they are irregular in outline, and in the beginning often contain a network of friable trabeculae with bile channels which escape destruction and which may still carry some fragments of softening liver tissue. In these early stages, the surroundings show a zone of whitish yellow color within which the liver tissue is infiltrated by pus, the lobular etching is thick, swollen and the liver cells are cloudy or undergoing fatty degeneration. In later stages, or when the abscess progresses more slowly, it is surrounded by a more or less vascular granulation tissue and finally by a fibrous membrane, often very firm, *i.e.*, it is encapsulated. Sometimes a large abscess the size of a child's head is found containing 2 litres or more of purulent yellow, or light yellow to milky, brown or chocolate colored material, sometimes of fetid odor (p. 915).

The color depends on the degree of fatty degeneration and the quantity of pus and blood in the admixture.

Sometimes a very large abscess (the author saw one the size of a man's head in the right lobe of a man 54 years old) develops from the confluence of smaller ones. In the case mentioned, the left lobe had undergone considerable compensatory enlargement and weighed 560 gms. The probable starting points were venous thrombi in the walls of diverticulae of the sigmoid.

Further Fate of Abscesses.— The abscess heals. The contents are partly absorbed, partly caseated, and eventually lime salts are deposited making them chalky. The cicatricial capsule contracts. Healing with pure fibrous stellar scars is rare. Abscesses may also perforate into the free abdominal cavity, into the pleural cavity, the lungs, bronchi, (evacuation of pus outward), pericardium, etc. Often the perforation takes place into preformed adhesions (pus sack), which secondarily rupture into the abdominal cavity, bowel, bile ducts, inferior vena cava, kidney, or through the diaphragm into the pleural cavity and its organs, even into the umbilical region, or through the abdominal wall at a more distant point.

Sometimes the abscess causes pyelothrombosis or phlebitis, and thrombosis of the hepatic vein. From the latter metastases reach the lungs and then the greater circulation.

Tropical (dysenteric) liver abscesses are found especially in the populations along tropical river bottoms. It rarely affects children and females. The abscesses are often very large, (may contain 8 litres of pus, Vaughan), solitary, and generally occupy the right lobe, because the trunk of the portal vein continues straight into the upper outer part of this lobe (Justi). Not rarely, however, multiple abscesses occur. As long as the abscess progresses, its walls are formed by an irregular, bulging, broad, necrotic tissue layer with tags floating in the cavity . Old abscesses may acquire a firm fibrous capsule (see Heubschmann). Generally icterus is present with pain in the hepatic region. The liver softens and fluctuation can be felt through the abdominal walls of thin individuals. The abscesses are mostly due to endemic dysentery, indeed frequently its lighter forms; the invasion of amebae is through the portal vein, or, according to others, more often through the bile ducts. An infectious gastro-duodenal catarrh is almost always present. Tropical liver abscesses are also named idiopathic or spontaneous, because the genesis is obscure in many cases. Kartulis and others found the ameba dysenterica in the abscesses and usually common pyogenic organisms as well (see p. 772). According to Justi, W. Fischer and others, the abscesses in amebic dysentery are more correctly necroses with pronounced tendencies to softening and purulent disintegration, but with practically no leucocytes. Pyogenic organisms may appear accidently. Sometimes healing has been observed, but perforation may take place (see above) into the lung in 53.7%, according to Justi (lit.). Goebel emphasizes the constant finding of liver cells in the pus which may be of diagnostic importance, if, for instance the pus is discharged per bronchi. Another valuable diagnostic sign is said to consist of scapulalgia, pain in the right shoulder (lit. to 1903 by Perutz; to 1906 by Goebel; see Br. Mel. #2495–1908 and Marchoux, Mac Callum, Scheube and especially Justi with excellent illustration and extensive lit.). Liver abscesses are much less frequent in bacillary dysentery.

Suppuration of the liver also follows purulent or ichorous thrombophlebitis of the portal vein (pyelophlebitis and pyelothrombosis) which in turn may be due to septic embolism from the introduction of softened thrombi, from spreading suppurative endophlebitis, periphlebitis or from periportal lymphangitis. The lymph channels along the ramifications of the portal vein are very numerous. The venous branches are dilated and filled with pus or with brownish green or greenish black thrombi; the vessel walls are dissected and the periportal tissue is infiltrated with yellow greenish or slate blue pus. The liver as a whole shows cloudy swelling and softening.

Occasionally the surface shows numerous small light dots and spots and only after section is the portal arrangement recognized. The surface may also show clay colored necrotic foci and dark red areas of congestion.

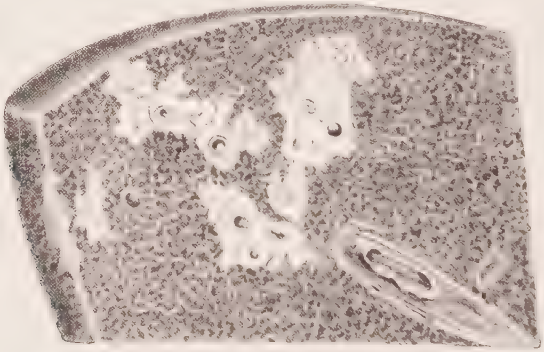


Fig. 438.—Pylephlebitic abscesses of liver, leaf-shaped arrangement; after appendicitis, man 24 years old. Below to right, a larger branch of portal vein with endophlebitis; within the lobular purulent foci branches of portal veins filled with purulent thrombi; liver tissue shows markings of engorgement. Nat. size.

The spleen is frequently much enlarged. At first there are elongated canalized abscesses following the branches of the portal vein, or leaf-like grayish yellow foci. The hepatic lobules can still be recognized but in time the liver cells, which are surrounded by bacteria-laden pus are destroyed and a green abscess results. The lobular abscesses become confluent and a cavity system is developed with many bulgings, filled with thick pus, sometimes fetid in odor. The vicinity is often discolored grayish green (iron sulphate). Otherwise, on the section surface light brown faded areas alternate with dark red angular circumscribed foci of liver tissue doubtless congested and necrotic from obliteration of portal vein branches.

Sometimes the inflammation extends to the veins (hepatophlebitis), from which infectious material may be carried into the lungs. Clinically a pyelophlebitis produces the general symptoms of pyemia (details by

Schottmuller). It may originate by (*a*) the direct introduction of organisms into the lumena of vessels emptying into the portal vein, *e.g.*, in perityphlitis via the superior mesenteric vein followed by thrombophlebitis which continues to the portal vein. In other cases bacteria are carried at once from the capillary system as emboli into the liver following which a retrograde infection of the portal vein may take place.

Pyelophlebitis may also develop by (*b*) continuity from neighboring organs, when pyogenic organisms invade the vessel from without and cause first phlebitis and then thrombosis. This pyelophlebitis may begin with a simple ulcerative process, or from an ulcerated gastric tumor, from the pancreas, bile ducts, gall bladder, kidneys, adrenals, even from the spinal column or ribs. In ordinary pyemia from a distant source, hepatic abscesses with periportal extension are also seen, but lung abscesses are almost always coincidently present. The process of development may be thus conceived. A collection of microorganisms which pass through other capillaries may settle in those of the liver because of the slow current; they multiply, reach the portal vein and cause (*c*) a thrombophlebitis. The embolus therefore need not be large.

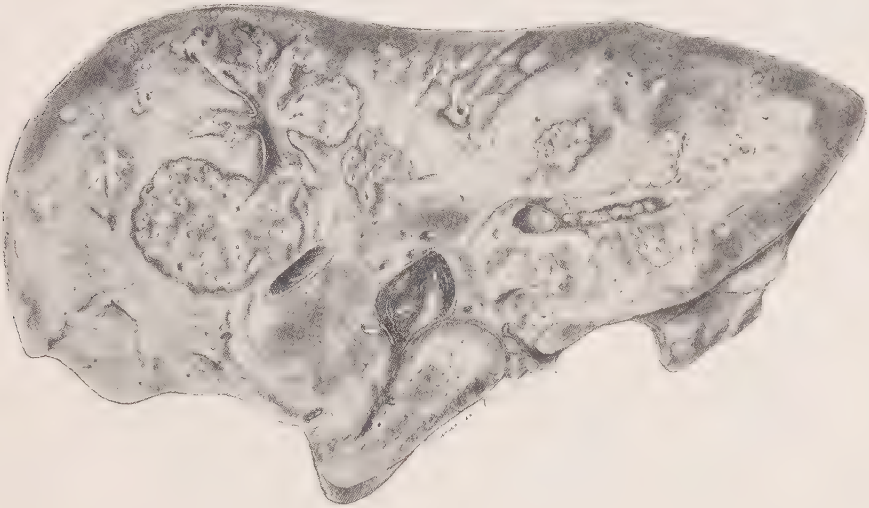


Fig. 439.—Portal abscesses of the liver with thrombosis and infarction. This was a suppurative pyelothrombo-phlebitis extending from an appendicitis. Innumerable abscesses were present throughout the liver, all in connection with the portal vein. To the right is a branch of the vein opened containing a thrombus. The discolored parts of the liver to the right are entirely necrotic, suffused with blood and infiltrated by pus cells. L. H. #50.

In the new born, infections of the umbilicus sometimes produce a phlebitis of the umbilical vein which sends some branches into the liver parenchyma to anastomose with intrahepatic portal twigs. Others enter the ductus venosus Arantii which begins to obliterate in the second week after birth (see Richter); straight continuations also lead directly to the inferior cava. Under pressure, pus flows from the vein at the umbilicus, and the trunk and the intrahepatic main branches of the portal vein may be filled with pus or sero-pus. Remarkable cases, also seen by the author, show peritonitis and metastatic abscess formation in the liver and other organs, but the umbilicus itself is unchanged and the phlebitis begins farther along in the vein (Durante and Buriner). The umbilical vein may only act as portal of entry into the liver without its trunk becoming involved. In one observation of the author, a three weeks old umbilical infection led to the formation of a system of abscesses in the Spigelian lobe in which the veins were wide, thick walled and filled with pus. Peritonitis and pyemia usually follow. Not rarely, numerous minute circumscribed or diffuse inflammatory foci are found which must not be mistaken for hemopoietic foci, (see Durante); nor must miliary hepatic abscesses, as well as those in the lungs, spleen, kidneys, etc. be mistaken for miliary gummata. Arteritis of the umbilicus with thrombosis is more frequent

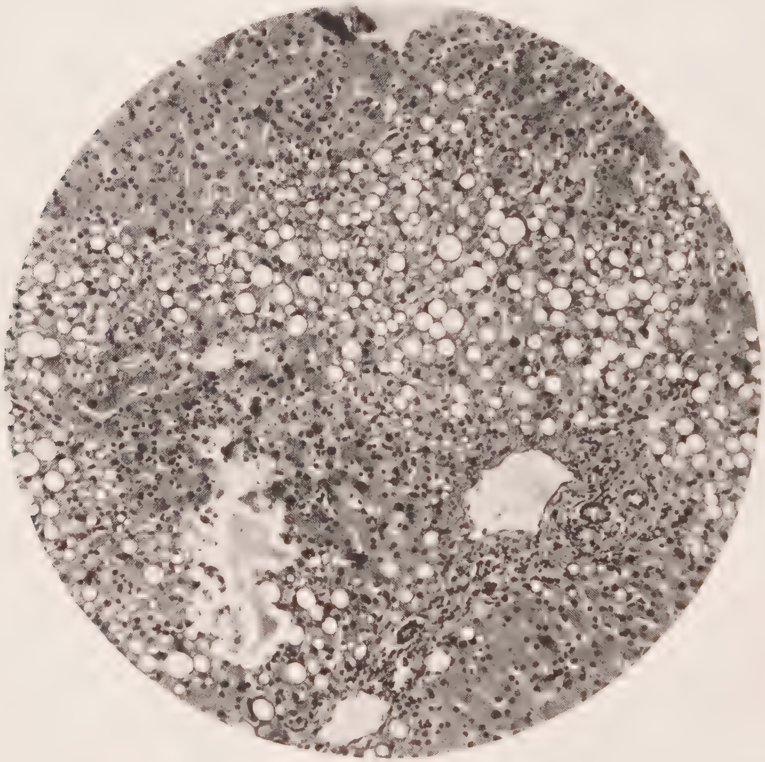


FIG. 440.—Periportal infection of the liver in the region of the gall bladder. The lymphatics of the gall bladder wall communicate quite freely with those in its bed in the liver and infection readily passes in either direction. This specimen from a patient aged 40 years with a suppurative cholecystitis. × 130. L. H. #126.

than phlebitis (see Runge): bacteriologically, the bacillus pyocyaneus has been found occasionally (M. Wassermann).

Umbilical infections may also cause injury to the liver by transmitting toxins which originate in an infected umbilicus and which cause fatty degeneration or even necrosis of the liver cells. The acute hepatic insufficiency produced may be followed by icterus neonatorum (see Durante).

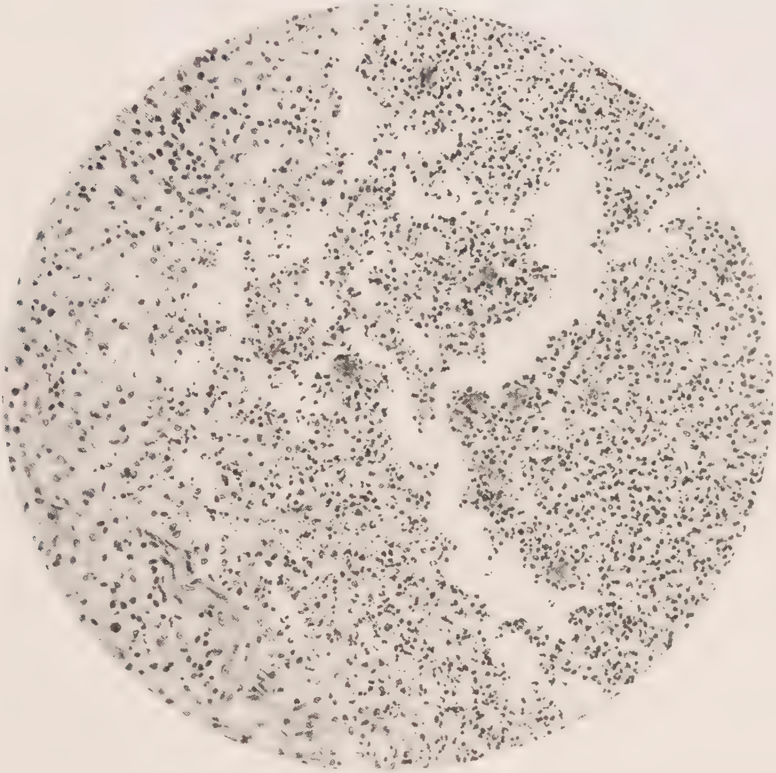


FIG. 441.—Suppurative thrombo-phlebitis. The wall of the portal vein is entirely disintegrated, its lumen filled with pus cells and bacteria. The patient had an acute suppurative appendicitis with thrombo-phlebitis of the meso-appendiceal veins. Extension upward and multiple abscesses of the liver. × 120. L. H. #210.

Hepatic abscesses are also communicated by way of the hepatic artery, but this origin is rare and appears mostly in general sepsis and pyemia, especially in ulcerative endocarditis.

Stuckey saw metastatic abscesses in erysipelas: most of the foci were small, miliary, often multiple, occasionally innumerable, mostly confined to isolated parts of the liver, though sometimes distributed among all lobes; as a rule they are unrecognized. They are situated beneath the capsule, or, as the author saw in a 25 year old woman (infected abortion, staphylococcus endocarditis), in a zone below it as thick as a finger. They begin as small, cloudy, grayish yellow infarcts penetrated by bacteria. If death does not result from the grave primary cause, the processes develop, and the capsule becomes cloudy and thickened. The author also saw small bile colored abscesses (secondary erosion into bile channels). In bubonic bacteremia, necrosing and purulent miliary and larger foci appear in the liver.

Hepatic Abscesses May Arise via the Hepatic Vein.—In very rare cases, infectious material reaches the hepatic vein by retrograde embolism (p. 893) as observed in thrombophlebitis of the dural sinus in conjunction with purulent otitis media, or in brain abscesses of traumatic origin, etc. The infectious masses travel from the dural sinus through a jugular vein, the superior cava, right auricle, inferior cava into the smaller ramifications of the hepatic vein (comp. Risel, lit., who reports the experimental production of minute retrograde embolic hepatic abscesses, see Reiniger critique and lit.). Hepatophlebitis may also develop after bacterial masses circulating in the blood and passing the capillaries, lodge in the central veins. In other cases, it is found in conjunction with pyelophlebitis or inflammation of the bile ducts.

Hepatic suppuration frequently follows inflammation of the bile ducts particularly in cholelithiasis. The inflammation ascends, communicates with the liver and bile channel and abscesses result. They are usually small and multiple, although larger, rounded, bile stained abscesses the size of peas or larger are found thickly crowded together. A single large abscess occurs but rarely. Peritonitis may follow when they are close to the surface.

The abscesses begin in purulent inflammations of the bile ducts which involve the interlobular connective tissue and the adjacent parenchyma. The cavities contain pus mixed with bile. It must be understood however, that inflammation of the bile ducts is but rarely caused by primary invasion of pyogenic organisms, (b. coli), from the intestines, but is usually secondary to injury by calculi or, more rarely, ascarides. Another starting point is in ulcerating tumors of the bile ducts (details under bile ducts). Bile stasis is very frequently combined, if calculi, or a tumor obstruct the ducts. In such cases all the lobes are filled with innumerable globular abscesses usually of the size of peas, but occasionally as large as cherries, which develop in some places in such thick groups that the liver on section looks like a sponge filled with greenish yellow pus, especially so because these abscesses often intercommunicate (multilocular abscesses). The remaining liver tissue is soft and its architecture is coarse and swollen. An observation of the author produced the basis of this description, (a 47 year old woman, calculus in common duct with septic symptoms for 8 weeks and icterus for 4 weeks; a general fibrino-purulent peritonitis followed the superficially situated translucent foci). If bile duct abscesses become chronic, granulations and later fibrous tissue separate the foci from the adjacent flattened liver cell columns.

The formation of an hepatic abscess following typhoid ulceration of the bile ducts is rare (see Venema, lit.).

The rare hepatic abscesses caused by invasion of ascaris lumbricoides (p. 852) were observed by Davaine, Scheuthauer, Leick, Saltykow, v. Saar etc., and Legrand calls attention to their relative frequency in children.

Liver abscesses may be due to suppuration of echinococcus structures, or to traumata, even in the absence of penetrating wounds (concussion); they are relatively frequent in children (Legrand) and post operatively. A simple gastric ulcer may extend to the liver in which a cavity is developed, due partly to the action of the gastric juice and partly to purulent softening of the tissue. Reactive production of connective tissue may lead to separation from the healthy surrounding tissue. Tumors of the liver rarely cause abscesses.

Chronic Interstitial Fibrous Hepatitis. Cirrhosis of the Liver.—Common atrophic cirrhosis of the liver; Laennec's cirrhosis; granular atrophy of the liver.

This form of chronic hepatitis depends on a marked connective tissue development with destruction of considerable liver tissue. The former is the most striking, and begins as focal proliferations around the branches of the portal vein (p. 923, fig. 444) in conjunction with lymphocytic infiltration. Microscopically, the usual sparse, narrow, connective tissue strands appear as broader cellular bands. As long as the granulation tissue formation exceeds the destruction of cells, the liver is enlarged, firm and heavy. This enlargement may be marked enough to designate it as a first or hypertrophic stage.

But in most cases this enlargement is not clearly manifested, indeed, some deny that it appears at all (see Cheadle). Some cirrhoses, nevertheless, especially in alcoholics, are combined with a permanent increase in volume. They may be called the "granular livers," and the reason may be a preexisting fatty liver, or a very active parenchymatous regenerative process. Cases are seen in which the surface is smooth.

The granulation tissue soon becomes contracting scar tissue and then a considerable part of the liver parenchyma undergoes atrophy (second stage). The liver is hard, difficult to cut, grates under the knife and the section surface shows but little blood and juice. The left lobe is the more reduced in size (fig. 442), and the total weight falls from 1200 to 900 gms. In a man 33 years of age, the author saw a cirrhotic liver weighing 880 gms., while the spleen weighed 500 gms. The section surface shows a network of macroscopically visible connective tissue (fig. 446). Since the fibres are connected with the capsule, the surface is retracted and granular (granular atrophy). The capsule is grayish white, cloudy and thickened in places. The surface granules may be small (size of pin heads and less) or coarse (like hemispherical shoe nail heads, hobnail liver) according to the width or narrowness of the inner meshes. Cirrhoses with very large bosses are always suggestive of lues. Exceptionally, the whole surface of the small organ or a greater part of it (a right or left lobe) is almost or completely smooth, but the section surface shows the distinctive picture of granular cirrhosis.

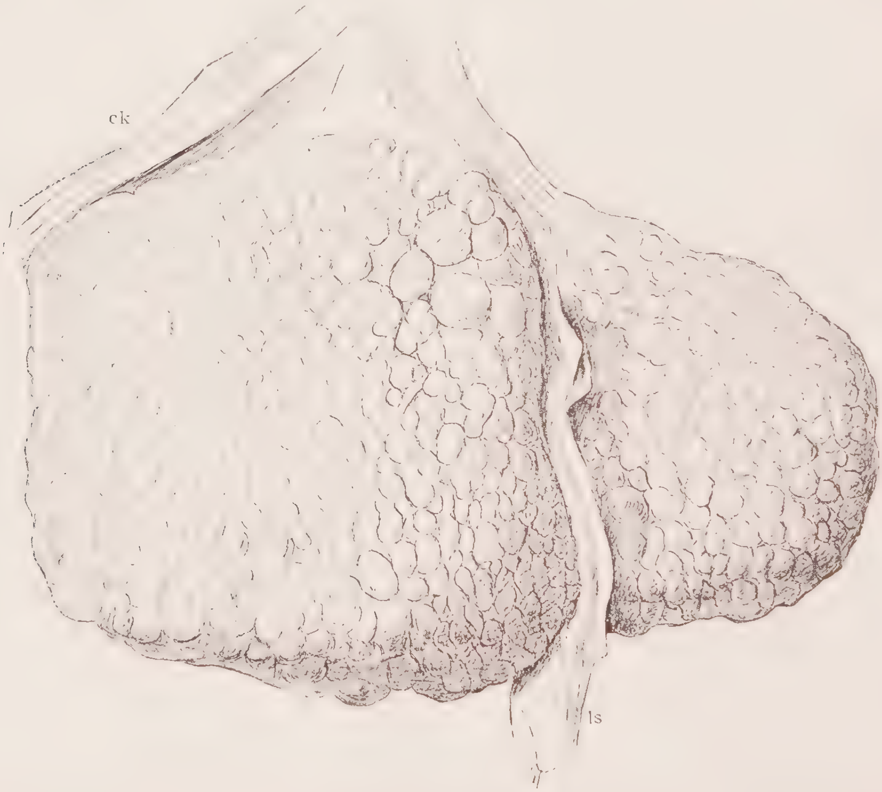
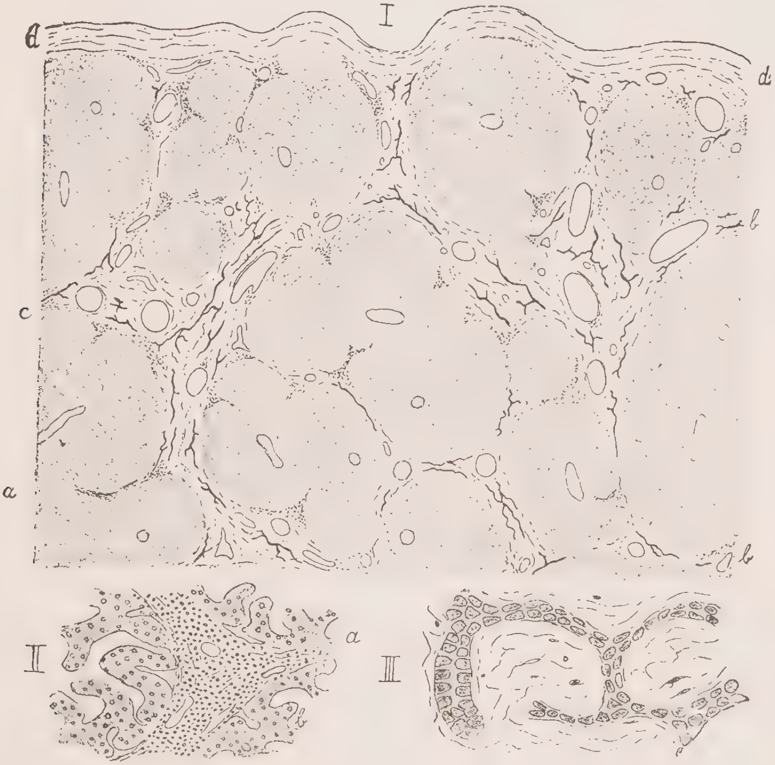


FIG. 442.—Atrophic cirrhosis of liver, from a drinker (spirits); unusually rough hob-nailed form; ls, suspensory lig.; lc, coronary lig; 4/5 nat. size.

The cellular strands which later become fibrous and richer in elastic fibres derived from preexisting connective tissue (Flexner), are grayish red in the beginning, and later pallid. They do not merely surround the individual acini, but penetrate into and through them by means of which they separate them at will, as rounded or ovoid patches, or islands of liver parenchyma, the so-called pseudo-acini.

Many speak of a multilobular form, but this name is not proper, because a monolobular form in which the connective tissue proliferation is carefully confined to the exterior of the individual lobule, does not occur; the granules do not represent the constriction of many whole lobules, but constriction of random pieces of many lobules. This has been demonstrated by serial sections in the peculiar, irregular forms of these pseudoacinar granules. The lattice fibres (see p. 886), are also said to proliferate in this cirrhosis (see Herxheimer); at all events, they are more closely drawn together, since the fibres are preserved but the liver cells disappear.



FIGS. 443-445.—I. Atrophic cirrhosis of liver; a, islands of liver tissue, composed of independent pieces and complexes of lobules; b, connective tissue with many wide vessels which can be injected from the hepatic artery; the black wavy lines are marked proliferations of bile ducts; c, small cell infiltration; d, thickened capsule of liver. Alum carmine stain. (Very low power.) II. Acute interstitial infiltration; a, cellular infiltrated periportal connective tissue; b, liver cell columns; in between are capillaries. Hematoxylin stain; (med. magn.). III. Proliferation of bile ducts in hyperplastic connective tissue in cirrhosis; above to the left, the transition of a very small newly formed duct into a larger interlobular bile duct. Hematoxylin stain. (High power.)

The process is not necessarily equally developed in all parts, and normal portions may alternate with diseased parts, especially in the early stages.

Often, the parenchyma when separated in these granules and penetrated by fibrous strands shows no coarse lesions; but again it may show atrophy (pressure atrophy) with concentrically compressed small liver cell columns with smaller cells, or, although the cells are of normal shape, they are abnormal in appearance from the infiltration of fat or bile pigment. On the other hand, there may occur an hypertrophy and also an hyperplasia with the formation of new liver cells which are recognized by their light protoplasm (bright cells, Kretz, Alder). Thus the liver cell columns are broader, the pseudo-lobules become rounded from within and jut out as tense yellow or greenish granules perhaps only the size of a pinhead, but frequently as large as lentils, projecting above the section surface almost like small tumors (adenomas) inside of annular grayish red or grayish white connective tissue strands. Sometimes the granular section surface resembles the pancreas.

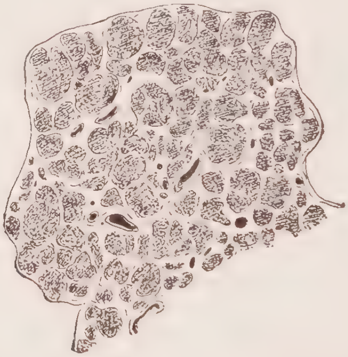


Fig. 446.—Atrophic cirrhosis of liver (granular atrophy); cross section of a piece from the Spigelian lobe; smaller and larger pseudo acini separated by connective tissue; nat. size.

The name "cirrhosis" is derived from the yellow color of the granules of the relatively normal parts. The peculiar changes in form of the granules probably depend not only on passive malformation from penetration of the original lobules and displacement of portions, but also on an extensive degeneration and reconstruction involving especially the capillary system (Kretz). This would cause the differences in size of the granules with larger ones in younger individuals, and likewise the transition to the tumor-like, rounded, hepatic islands and the nodular hyperplasias without typical lobule formation seen in some cirrhoses. The liver cells show evidence of proliferation in the form of enlargement, with large, and often multiple nuclei and these changes are frequently most active in the peripheral parts of the nodules, where several cells may occupy the width of the colmun. de Leeuw, however, believes these are not signs of compensatory hyperplasia.

Cirrhosis, yellow, gave the name to the contracted liver, but this term was later applied generally to organ shrinking processes which are accompanied by more or less formation of connective tissue such as in cirrhosis of the lung or of the kidney. The color is then ignored.

Numerous smaller branches of the portal vein and the smaller bile channels are wholly or partially obliterated by the connective tissue. The latter causes bile stasis and bile pigment precipitation in granules and clumps. To compensate for the loss of portal veins, an enlargement of branches of the hepatic artery takes place which appear as delicately-walled, wide gaps in the connective tissue (p. 923, fig. 443).

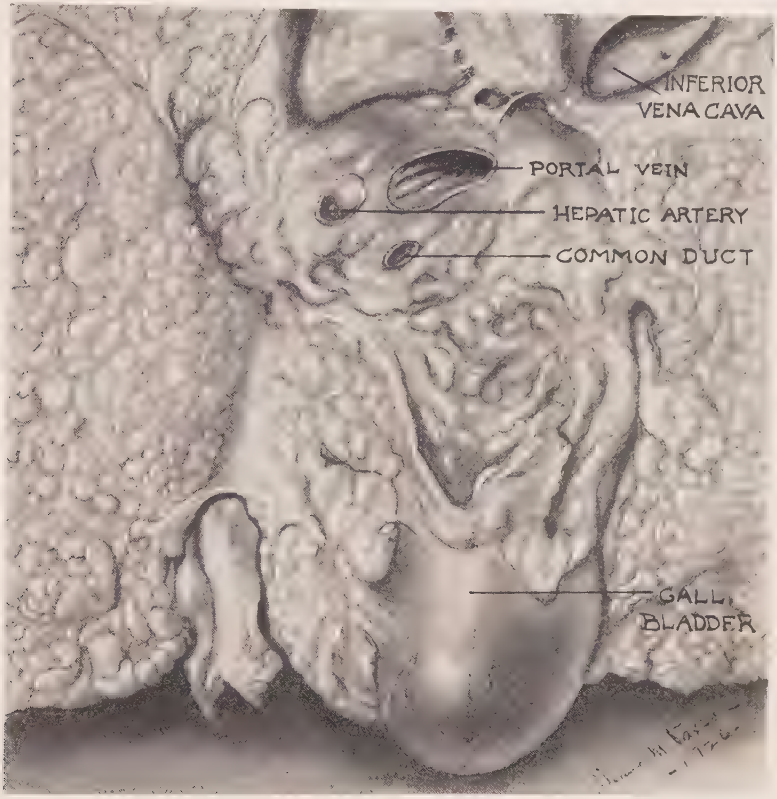


FIG. 447.—Marked cirrhosis of the liver. Inferior surface. From a patient 54 years old. This patient had severe diabetes and before death was markedly jaundiced. The type of cirrhosis is periportal. There were a small amount of ascites and considerable passive congestion of the viscera drained by the portal vein. The color of the connective tissue bands separating the lobules is light gray, that of the lobules which jut out far beyond the surface of the connective tissue is yellow green from fatty changes and from jaundice. L. H. #146. ⅝ nat. size.

More remarkable, however, is the development within the connective tissue of numerous, long, convoluted and branching tubules lined with epithelium, the so-called bile duct proliferations which appear more or less plentifully in all forms of chronic inflammatory processes (p. 923, fig. 445). These canaliculi may be injected from the common duct (Ackermann), but they also change directly into liver cell columns at the other end. Hayami (lit.) disputes this latter statement, and considers the so-called transition pictures as secondary junctions with preexisting liver cells. They are, however, newly formed canaliculi developed by budding from the normal interlobular bile canaliculi just as they evolve from proliferating bile channel epithelium during hepatic regeneration after trauma. This latter statement is supported by their long branchings and convoluted courses (p. 923, fig. 443). Numerous canaliculi lying side by side may simulate the picture of adenoma. It has also been asserted that such channels may be produced by the differentiation of liver cell columns (Orth, Goldzieher and V. Bokay, see Herxheimer and Gerlach also).

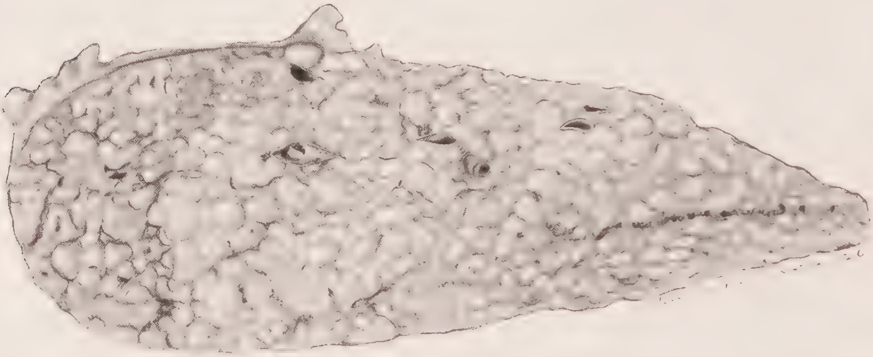


FIG. 448.—Cross section of the same liver as in fig. 447 showing that the process was quite diffuse. ½ nat. size.

Very often, in fact in about half of the cases (Krotz), hemosiderin (iron reaction p. 372), is found, perhaps in large quantities in both the connective tissue, especially in periportal situations and in the liver cells themselves. In suppurative conditions the interstitial tissue may be colored macroscopically gray to deep blue green by the action of sulphuretted hydrogen on the iron-containing pigment. It was formerly thought in the cirrhoses with much hemosiderin, that hemorrhages in the digestive tract were the prominent cause of the deposit. Kretz theorizes that the pigment is liberated by abnormal chemical destruction of erythrocytes. This unknown noxa, possibly a metabolic product induced by alcohol, is supposed to reach the liver with the blood pigment thus causing both cirrhosis and pigmentation. Bleichroder thinks hepatic cirrhosis is a blood-borne disease due to changes occurring in the sources of the portal vein.

Pigment cirrhosis is also observed in some cases of diabetes mellitus (diabete bronze, Hanot and Chauffard). In the majority of these cases (Anschutz lit.), there is coexistent pancreatic cirrhosis with pigmentation, and while the liver is usually enlarged it is more frequently distinguished by its hardness than by its macroscopic granulation. The author saw weights of 3000 gms. and more (s. I Diss. Prize essay). General hemochromatosis (v. Recklinghausen) with brown discoloration of skin and internal organs (spleen, kidneys, lymph nodes, mucous and serous membranes, the heart, thyroid, etc.) also occurs. Vessel sheaths, skin glands, fatty tissue, bone marrow (in marrow cells), etc., are also involved (for

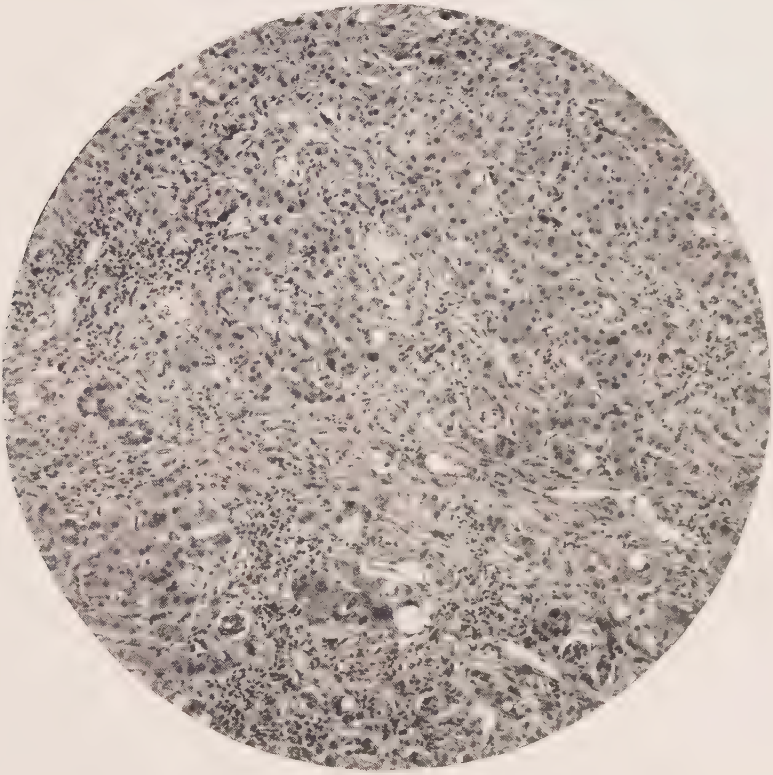


FIG. 449.—Biliary cirrhosis of the liver. This is the type of connective tissue increase which occurs in chronic infection and obstruction of the bile ducts. It is a so-called liver of "surgical delay," *i.e.*, delay in removing gall stones and infected gall bladder. Occasionally, however, an acute cholecystitis will be followed by infection of the bile ducts in so rapid a sequence that therapy is unavailable. In the acute cases, multiple biliary abscesses are quite common. It is also quite possible that such biliary infection can be produced by the excretion into the bile of organisms from the blood of the portal vein. There is general connective tissue increase everywhere within and around the lobules. It is so uniform that hob-nails are not produced because the periportal increase is not overbalancing. In addition, there are, as shown, the cells of chronic inflammation. There is a certain amount of hyperplasia of bile ducts in this type also, but in the translator's experience not to the extent as present in ordinary atrophic cirrhosis. In animal experimentation, complete obstruction of the ducts of one lobe is followed by fibrous atrophy to complete extinction of the parenchyma of the lobe. As long as sufficient portion of the liver is allowed to function, however, death does not result. This portion varies, but when the remainder of the liver is healthy, it is said that nineteen-twentieths of the ducts of a dog's liver can be tied off without producing death. There are of course hypertrophy and hyperplasia of the functioning lobe or a portion of the lobe. × 110. L. H. #160.

more details, see Preiswerk, lit.). The intercellular pigment usually gives the iron reaction (hemosiderin); a smaller part is free from iron and may be hemofuscin, but according to Hueck, it is lipofuscin derived, not from hemoglobin, but perhaps from lipoid substances in the erythrocytes. This combination is the characteristic mark of differentiation from hemosiderosis. The relation between diabetes and pigment cirrhosis has been conceived as follows; the excess of iron comes from erythrocytes destroyed by the same noxa which causes the cirrhotic processes in both the liver and pancreas, *i.e.*, there is a primary alteration of the blood (abuse of alcohol, according to Simmonds), but this seems doubtful (Letulle, Kretz). Perhaps a diminished excretion of iron necessitates storage in the tissues (Anschutz). According to Murri, who is joined by Hess and Zurhelle, chronic disturbances of the general metabolism cause both an increased capacity of the tissues to take up pathological amounts of liberated blood pigments (hemochromatosis) with increase of hepatic connective tissue (cirrhosis), and a diminished power of the cells to oxidize carbohydrates (diabetes). Others are of the opinion that it is merely a combination of hemochromatosis with cirrhosis (see Piery), or a disturbance of the iron metabolism (siderosis, Quincke, Nienhold) appearing fortuitously in diabetes when the liver of a diabetic accidently becomes cirrhotic (Wateau). In contradistinction to simple siderosis (hemosiderosis), which is found in various conditions, Chrostek explains the combination of general hemochromatosis with cirrhotic changes in the liver by diseases of the spleen and pancreas. The liver and spleen control normal hemolysis and are the decisive organs in iron metabolism. As a third organ, the pancreas is added which may liberate an hemolysin into the blood under certain conditions. This creates an abundant supply of pigment, and because of changes in the iron metabolism, abnormal substances which cannot be utilized may be formed and deposited with normal pigments (more in reference to bronze diabetes by Rossle, Potter, and Milne, Ungeheuer).

> **Translator's Remarks.** According to Mallory (Arch. Int. Med., 37:336, 1926) evidence is slowly accumulating to show that hemochromatosis, bronzed diabetes and pigment cirrhosis are caused by chronic copper poisoning. The metal is ingested in the food, which, if slightly acid, dissolves some of a copper utensil in which it is mixed or cooked.

Consequences of Atrophic Cirrhosis.—As a consequence of granular cirrhosis, there may be passive congestion from compression of the portal vein and obstruction to capillaries displaced from their normal positions. Splenic tumor, chronic congestive catarrh of the stomach and intestines, and serous exudation, *i.e.*, ascites, are other results. Often—in about 10% of the cases—tuberculosis of the peritoneum is found; the ascites is hemorrhagic at times. Intrahepatic collaterals between branches of the portal and hepatic veins are of little use contrary to Sabourin's ideas (see lit. by L. Pick), but as mentioned before (p. 894), extrahepatic collaterals are opened and lead, in rare cases, to a caput medusae (p. 165, lit.). These pathways are not sufficient to prevent serious consequences. The collaterals vary in individuals (Thomas); the following are the most frequent routes: portal vein, left coronary vein, superior esophageal veins, intercostal veins, azygos vein (*i.e.*, hemiazygos) and the superior vena cava. For more details in reference to hepatofugal collateral tracts in cirrhosis, see L. Pick, and p. 894.

Talma's operation of fixation of the omentum in the abdominal wall (omentopexy) is designed to make new collaterals between the portal vein and the greater circulation, and also to partially obliterate the peritoneal cavity so that collection of ascitic fluid is prevented. Such collaterals may also form spontaneously (see Rossle, lit.). There is the possibility of fatal hemorrhages from the gastric and intestinal mucosa, (see p. 664), or from dilated esophageal veins (p. 633). Icterus may follow pressure by the connective tissue on the smaller bile channels and, according to Eppinger, intracellular ruptures may occur from stenosis of larger channels in the connective tissue, or from gastro-duodenal catarrh, or perhaps from inflammatory changes in the ducts (see Naunyn). The icterus is usually moderate and may be entirely absent. Bleichroder considers it hematogenous. If the portal vein becomes thrombosed — a rare complication — the ascites increases rapidly.

Hypertrophic Cirrhosis of the Liver (with Icterus), Hanot's Cirrhosis.— The cirrhosis just described is known as Laennec's cirrhosis or granular atrophy. It has been mentioned that the liver, as a whole, is often enlarged in the first stages (see p. 921), but this "hypertrophy" is by no means a constant feature of the developmental cycle, so that cirrhotic livers with marked fat infiltration, and thus enlarged, enlarged pigmented livers in bronze diabetes showing otherwise the types of structure found in Laennec's cirrhosis cannot be called "hypertrophic cirrhosis." A true hypertrophic cirrhosis depends on a productive inflammation characterized by marked progressive enlargement, until the liver is 50 cm. in breadth, and an increase in weight to double the normal (4 kilos); the consistency is tough, but the surface is fairly smooth. The section surface has no lobulations, is grayish red, or green if stained by bile pigments. The disease is chronic and gives attacks of pain in the region of the liver, is almost always accompanied by icterus and fever, although sometimes only in the later stages; the feces contain bile. Young males are the usual victims. Generally, the splenic tumor is larger than in Laennec's cirrhosis (up to 600 gms. and more, see p. 224). Ascites may be absent to the end. When the disease is protracted, a hemorrhagic diathesis is apt to appear.

Microscopically, the boundaries of the lobules are not recognizable since they are penetrated by connective tissue which appears between them as broader strands, and in them as a fine network between the cell columns, separating them into smaller cell nests, indeed almost into isolated single cells. This connective tissue retains its nuclei for a long time and does not contract, or only very late in the disease; it is "elephantoid" (Ackermann). It is this intraacinar diffuse connective tissue proliferation which differentiates hypertrophic cirrhosis from granular atrophy. The compressed liver cells usually containing fat and bile pigment become smaller and tend to disintegrate in places, leaving a pigmented debris. In other places, liver cells are especially well preserved and are probably regenerated from remaining fragments of parenchyma (karyokinesis, Prus). The bile channels proliferate to more or less degrees and may, as in Laennec's cirrhosis, resemble adenomas. The smaller channels may be overfilled, the larger passages sometimes are surrounded by whorls of vascular connective tissue, their epithelium is desquamated and perhaps proliferated. Some authors, such as Charcot, believe this is the starting point of the whole disease (see H. Heineke, Eberth), but it seems better to designate only such cases as Hanot's type, which are not complicated by capillary cholangitis (Kretz).

Etiology of Cirrhosis of the Liver in General. There is less information available as to the cause of hypertrophic cirrhosis, although infections and toxemias are implicated (see under tuberculosis), than of granular atrophy in which toxic factors such as alcohol, and especially brandy, are recognized. Although formerly overrated, nevertheless, according to the opinion of many authors, alcohol plays an essential predisposing part, but unquestionably infections must also be taken into consideration.

The author performed an autopsy on a boy 15 years of age, who was a notorious whiskey drinker and found typical cirrhosis with all its symptoms, splenic tumor, ascites, etc.

Statistically, a history of alcoholism is found in about three-fourths of all cases of cirrhosis of the liver (see Simmonds and Klopstock, lit. Kern), but on the other hand, only a small fraction of alcoholics develop cirrhosis of the liver, indeed for the most part they have fatty livers or no changes at all (see Fahr). But cirrhosis may develop in a fatty liver (see Kern), and thus there results a fatty cirrhosis (cirrhosis with marked fat infiltration).

Opinions are divided in regard to the direct action of alcohol itself on the liver, or to its indirect action through gastrointestinal disturbances

(Boix), especially by the formation of fatty acids, such as butyric acid. These produce dyspeptic or enterogenous autointoxications as causative factors; the alcoholism is thus the predisposing cause (Klopstock). Feeding these acids and other acetone-forming substances to rabbits often resulted in certain interstitial changes of the liver (Poggenpohl, lit.), although not usually in typical cirrhosis (D'Amato and Joannovics, lit.). Lissauer records better results obtained by feeding decaying material, such as broth from decomposed meat. Chalatow claims he produced cirrhosis by cholesterin feeding.

The older attempts to reproduce the disease by long continued alcohol intoxication gave contradictory results, but in the majority, no effects (lit. by Klopstock, Poppenpohl, Saltykow). v. Baumgarten (1907), in fact, denies that it has an effect on the liver, even in large doses continued over long periods of time. Schafir (lit.), on the other hand, found an increase of lattice fibres in rabbits and deduces from this that alcohol has a "cirrhogenous" action (see also Grower). In later experiments, (Lissauer, lit.), large doses of alcohol given to rabbits intravenously, per os, or subcutaneously, no doubt caused cirrhotic changes, but not in all cases in carefully controlled experiments, which convinced Kryle and Schopper that a special predisposition must be present in positive cases. These workers, like Jaffe, believe that there must be some previous injury to the liver parenchyma. What has been known for a long time must be remembered in judging results, viz., that cirrhosis may appear spontaneously in rabbits (see Klopstock, Beitszke).

Experiments with other poisons also gave inconstant results. Chloroform was used by inhalation and subcutaneous injection (Jaffe), also toluylendiamin, ammonium carbonate, etc. There was seen a combination of parenchymatous degeneration, interstitial tissue proliferation, and regenerative hyperplasia of the parenchyma.

The liver cirrhosis of horses and hogs is also considered due to an enterogenous autointoxication (Mugler, lit.; see Joest). In reference to syphilis and acute infections, see below, and p. 928.

The character of the histological process permits of several interpretations. Formerly, most workers stressed the interstitial inflammation; others considered the process a combined progressive degeneration and "sclerogenous" injury (Siegenbeck van Heukelom); Kretz lays emphasis on the primary destruction of cells believing that cirrhosis of the liver is the anatomical result of a constitutional disease which injures cells as a focally localized, exacerbating, chronic degenerative process with intercurrent regenerations of parenchyma. MacCallum, and also von Gourevilsch, consider the degenerative processes as primary and the latter describes fatty degeneration, more rarely necroses, as initial changes. But the author thinks that assigning only a reparatory action to the connective tissue proliferation is going too far; it might, indeed, be nearer the truth to take sides with Siegenbeck van Heukelom, and believe that the noxa causing the whole disease produces a degenerative injury to the more delicate liver cells, and also stimulates the production of interstitial connective tissue (Kyrle and Schopper). According to the kind of deleterious agent, one or the other process would predominate. Regenerative new formation of liver cells and incidental bile channel proliferations are then added (see Oertel, Geraudel, Piery, references by Fischler, lit.).

Cirrhosis usually appears in middle life and is more frequent in men. Syphilis, even the congenital form, may cause an ordinary, or an especially coarse grained, more focally arranged cirrhosis, and possibly the hypertrophic type also (see p. 929), which occurs even in childhood. M. Letulle has recently reemphasized the frequency of the syphilitic origin.

Some of the cirrhoses of childhood (Lewerenz, lit.) are caused by acute infections such as scarlet fever, measles, etc., (lit. by Bingel) and are combinations of parenchymatous degenerative changes, connective tissue proliferation and regenerative processes of the Laennec's type.

Some consider tuberculosis a frequent agent (Piery, and especially Schoenberg, lit.), but others treat this view skeptically, or refuse to accept it at all (Kern and Gold). Kirch believes that few of the cases mentioned in the literature as tuberculous cirrhosis are definitely proved, but gathers from his own observations that cirrhosis of the liver of a pure tuberculous origin is possible, with its beginning in an interacinar tuberculous granulation tissue proliferation. We ourselves cannot deny that tuberculosis may produce changes which finally resemble Laennec's cirrhosis (see p. 936), yet the combination of the two is by no means frequent. Lorentz found only 16 cases of tuberculosis mentioned as the chief finding in 111 cases of cirrhosis (Kern and Gold, Blumenau).

Kretz thinks that the cirrhoses of young individuals show larger granulations since he found parenchyma islands of the size of peas and beans, but this is no strict rule. The author has preparations from eight and ten year old girls with typical uniformly small granular nodules (one liver 645 gms.—spleen 210 gms. and the other liver 450 gms.). The genesis is obscure, but certainly not luetic.

Osler never believed that malaria could produce a typical cirrhosis such as French authors have described (Kelsch and Kiener, Ughetti, Tucker). Marchiafava and Bignami (lit.) found severe simple atrophy in the liver in chronic malaria, changes fundamentally different from those in Laennec's, as well as in hypertrophic cirrhosis with icterus.

There are cases in which the first change is extensive necrosis of liver cells, later followed by connective tissue production, *e.g.*, in chronic phosphorus poisoning, or chronic infectious bile stasis with cholangitis and pericholangitis following occlusion of the large bile ducts by calculi or tumors, (10 times in 80 cases of carcinoma of the hepatic duct, Rocco). In the latter condition the connective tissue proliferation may assume massive proportions and lead to a type which has been called biliary cirrhosis, or calculous cirrhosis, or obstructive biliary cirrhosis. Necrotic foci appear in the hepatic lobules and bile channel proliferation occurs with inter- and intralobular connective tissue formation (see Janowski and Ogata's experiments). This liver can be distinguished from that of Hanot's cirrhosis even macroscopically, by the coarse inter- and intralobular knotty fibrous strands, or softer granulation tissue tracts penetrating the dark, icteric liver tissue. These granulation tissue tracts may be rich in bile channel proliferations. Moreover, the liver is harder, grates on cutting and changes, after a preliminary increase in volume which occasionally doubles the weight, into a cirrhotic, coarse grained atrophy, while in Hanot's cirrhosis the enlargement is progressive. Ascites is rare, and the splenic enlargement is moderate.

The change designated as "cirrhose cardiaque" seen in the congested liver has been mentioned on p. 892. Another form occurs which might be called indurative or smooth cirrhotic atrophy in which the contraction involves all parts similarly, and no sharply marked granular bossing appears on the outer or on the section surface. The picture is distinctive only on microscopic examination.

The type in which the serosa is thickened, often to several millimeters, and is fibrous, warty, or smooth and hyalin over a non-cirrhotic, usually soft liver is called chronic fibrous or hyperplastic perihepatitis (zuckerguss liver). It may lead to increased density, decreased volume by pressure (without congestion), and changes in form (cake shaped). As in cirrhosis, the portal vein may be obstructed and ascites and splenic tumor appear. Sometimes the splenic serosa or even the whole peritoneum (p. 668), sometimes the pericardium—which usually shows many adhesions, and the pleura—when the lungs may show multiple lobe deformities—also show smooth cicatricial hyalin thickenings. This may be primary or secondary, *i.e.*, starting from the pericardium or the right pleura, or it may extend from the abdomen to the pleura and pericardium. The author saw, among others, a case in a 60 year old woman in which the process was combined with the formation on the peritoneum of numerous chylous lymph cysts up to the size of a fist. Peck speaks of pericardial pseudocirrhosis of the liver, and he sees the primary change in an obliterating inflammation of the pericardium, especially in narrowing of the mouth of the inferior vena cava, thus producing congestion, not general, but of the liver and portal circulation alone, which leads to thickening of the serous coat of the abdominal viscera and causes ascites. But no doubt this is quite different from zuckerguss liver which is caused by an inflammatory, perhaps infectious process. Both show frequent obliterating pericarditis (Siegert, and our own observations; lit. by Nocholls, Huguenin, Rose, Hess). Huebschmann assumes, generally speaking, that there are two factors in the development of zuckerguss liver, first, an impairment of the hepatic blood circulation due in his case to a chronic tricuspid lesion, and second, inflammatory changes, in his case due to slight infection following frequent paracentesis for ascites. Pericarditis and polyserositis do not necessarily always coexist.

Very rarely a thick, hyalin, porcelain-like coating is seen over a true cirrhotic liver, as the author saw in a 51 year old man, (p.m. 145, 0.3 Basle), whose liver weighed 2285 gms. and spleen 442 gms. (comp. Reiner).

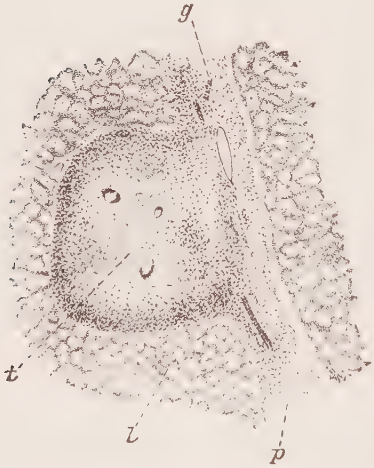


FIG. 450.—a. Tuberculosis of liver. Conglomerate tubercle (t) with caseation and three giant cells, macroscopically resembling a miliary nodule; g, bile capillary; p, periportal (interlobular) tissue, shows marked small cell infiltration; l, liver cell columns; (low power).

Infectious Granulomatous Tumors

Tuberculosis.—Tuberculosis of the liver, usually without clinical symptoms, is secondary almost without exception and appears in various forms.

Miliary and submiliary disseminated tubercles are the most frequent manifestations: they are grayish white and may become confluent. They are often so small that they are discovered only microscopically (fig. 435, p. 902).

The smallest nodules are only lymphocytic; larger ones contain epithelioid cells, caseation, and giant cells. The tubercle bacilli select the interlobular connective tissue, in which a more or less marked interstitial inflammation and bile channel proliferation develop. The bile channel epithelium may be converted into giant cells, as first demonstrated by Arnold. From here the bacilli spread into the peripheral parts of the lobules destroying the liver cells en route, while, not rarely, the liver tissue shows a concentric arrangement, similar to that around a carcinoma nodule. But quite frequently the organisms settle in the lobules in the very beginning. The macroscopic tubercle is microscopically usually conglomerate (fig. 450).

See the experiments of Oppenheimer (lit.), who asserts that the stellate cells are the matrix of all epithelioid and giant cells, and Miller who thinks giant cells are derived from endothelium, and Wallgren who believes giant cells result from a fusion of lymphocytes or smaller polyblasts, or of epithelioid polyblasts, but denies the association of stellate cells which he thinks perish; Schilling believes that the stellate cells participate directly or indirectly in the formation of tubercles around the first colonies of bacilli.

The dissemination of tubercle bacilli may be hematogenous as in acute generalized miliary tuberculosis in which the liver is swollen from the immense number of tubercles. In the chronic forms, they can almost always be found in extensive pulmonary tuberculosis, especially when tuberculous intestinal ulcers are also present. But lymphogenous spread must also be remembered, just as in carcinoma. Glaus described a case of isolated miliary tuberculosis of the liver, from tuberculosis of the splenic vein and chronic caseous tuberculosis of the pancreas. The liver caught the bacilli as in a filter (see also a case of M. Massini).

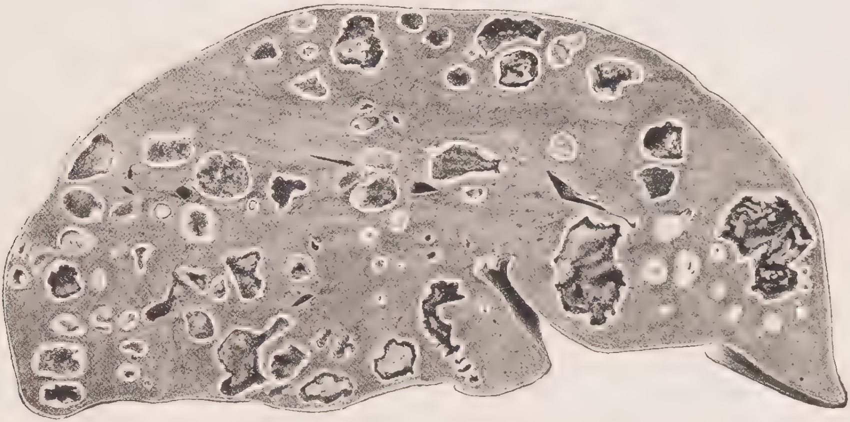


FIG. 451.—b. Tuberculosis of bile ducts with formation of numerous cavities; girl 5 years old (with tuberculosis of lungs, bronchial nodes, kidneys); ⅔ nat. size.

More rarely, we encounter larger foci up to the size of peas, which are firm, caseous, of icteric color, and contain a small ulcerative cavity within filled with caseous fragments and bile stained material. These are the so-called bile channel tubercles, and macroscopically are quite different from disseminated miliary nodules.

The difficult question in reference to the formation of bile duct tubercles has been variously answered. According to Kottar, whose findings were verified by Lichtenstein in the author's institute, the tubercles extend from the vicinity to the walls of the bile channels. According to Simmonds, who taught the theory of hematogenous excretion tuberculosis (especially in relation to tuberculous tracts in the male genitalia), the inner surface of the bile channels is infected by tubercle bacilli excreted in the bile. The idea is contradicted by Sussig, and Joest and Emshoff, on the basis of investigations in tuberculous animals; they do not believe in excretion tuberculosis, saying that the bacilli would have to come from tuberculous changes of the liver; however, Joest now admits, what is self evident, that if tubercle bacilli have once reached the bile channels, tubercles may form in their walls. By caseation and ulceration, a cheesy channel gradually becomes an ulcerative cavity by progress outward and decomposition within.

In this way, in rare cases, cavities develop to the size of a cherry (fig. 451). Microscopically the lining of the wall is not of tubercles but caseous material. The preparation pictured in fig. 451 is unusual, the whole liver presented large and small cavities, the walls were 1–1.5 mm. thick, caseous and bile-stained, the contents fluid and caseous material.

Bile channel tuberculosis may also be called tubular tuberculosis in analogy to caseous bronchitis, deferenitis, salpingitis, etc. The cavity may purify itself, become a sort of cyst, or, even in rare cases, heal by fibrous tissue.

Larger solid conglomerate tubercles run a chronic course. They are rather rare, but appear relatively often in children, frequently following peritoneal tuberculosis. Occasionally secondary cavities form by softening of the interior of the nodules.

Jenny points out that encapsulation of tuberculous foci is not at all uncommon.

Unusual Forms.—Large tumor-like conglomerate tubercles reaching the size of walnuts or even fists, of soft caseous constitution, are seldom seen (Orth, Simmonds, Sigg, lit.; W. Fischer, Pertick, lit. Krause, E. Fraenkel, Brutt, etc.). It is easy to confuse these with gummas and the demonstration of bacteria is necessary for proof.

Cirrhosis of the liver on a tuberculous foundation corresponds mostly to the picture of Laennec's cirrhosis (p. 932). It has been observed in numerous cases of tuberculosis in animals (lit. by Stoerk, see Wallgren, Klopstock). The hypertrophic form is rarer, and the liver may acquire enormous weight (in a case of Isaac, 9470 gms.). The bacilli and tubercles may be found, and very occasionally, larger caseous nodules.

Wegerle describes an unusual case of subacute atrophy of the liver with nodular hyperplasia on a tuberculous base.

Rossle, in a case of tuberculosis saw liver giant cells with many nuclei, but no bacilli or tubercles in the liver.

According to Eberth's conception, bacillary pseudotuberculosis is the process in which tubercle-like nodules are found in the liver in isolated newborns (streptobacillary pseudotuberculosis, Aschoff). In adults it may be mistaken for metastatic carcinoma. The nodules consist of cellular granulation tissue with a tendency to necrosis, and the bacilli found belong, with slight differences, to the group of Pfeiffer's bacterium, *i.e.*, pseudotuberculosis rodentium (Roman, lit.).

Syphilis of the Liver (see fig. III, p. 464).—Syphilis causes various forms of interstitial inflammation as well as specific granulation tumors, or gummas (see microscopic illustration of a gumma, fig. 64, and under muscles). Congenital, *i.e.*, intrauterine syphilis of the liver presents a very different appearance from the acquired variety and is especially rich in spirochetae.

Spirochetae are found not only in parts showing changes in structure, but also in places where changes are not demonstrable.

In congenital syphilis of the liver, which is very frequent, especially in comparison to that of adults, two types may be differentiated, which sometimes combine.

(*a*) **Interstitial syphilitic hepatitis** consists of connective tissue proliferation, either diffuse, or, more rarely, striated. With diffuse connective tissue proliferation, the organ is quite large, firm, elastic with a smooth surface; the section surface is smooth, without design, sometimes, especially if the child was born at term, of light brownish gray color, and glassy, slightly irregular, consistency (flint-liver). The older the fetus, the more pronounced the condition. Microscopically, a loose, fine fibrillar connective tissue with abundant spindle cells is deposited in the parenchyma, either in foci or diffusely (fig. 452). The diffuse and fine distribution disarranges the structure of the liver and the architecture is disturbed. Liver cell columns are often recognized with difficulty because of atrophy, or remain as isolated liver cell remnants. The connective tissue development as found by examination in the early stages, is intraacinar around the capillaries (fig. 452). Later, this arrangement is not so apparent in ordinary microscopic sections, but Erdmann could demonstrate this relation, which includes fibrillae surrounding the capillaries, in quite advanced stages by his "digestion" preparations. Many capillaries are completely covered with connective tissue. In such a liver caseous gummas and cellular infiltrations may also appear in large numbers. In contradistinction to this purely hyperplastic connective tissue proliferation, the second form, studied by Erdmann, leads to the formation of single strands or striae of

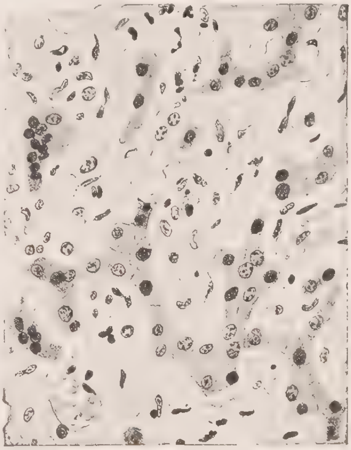


FIG. 452.—Congenital syphilis of liver. High power; see text.

connective tissue, rich in round and spindle cells and sprinkled with newly formed bile channels. This arises from the supporting tissue of the large vessels and of the liver capsule as in inflammatory proliferation. Rays penetrate the parenchyma and cause slight contractions on the surface. The organ may be normal in size, but firm in consistency, and while the diffuse form represents a parallelism to hypertrophic cirrhosis, the last mentioned form suggests a transition to a lobulated liver, or to a common cirrhosis. Strassburg thinks that diffuse increase of lattice fibres is specific of congenital syphilis.

In some cases the liver is dark brownish red and enlarged, but soft and the lobular design is preserved; the tissue is invaded by hosts of various kinds of cells most noticeably in the capillaries, but also around them, and in the periportal connective tissue, or even jammed between the liver cells, where they form circumscribed foci, appearing under low power somewhat like lymphomas. Larger cells with weakly stained nuclei and many smaller round cells with deeply staining nuclei are also seen. The whole constitutes a marked cellular infiltration. If this picture is not marked, it is inadvisable to diagnose syphilis from the liver findings alone, because such cell infiltrations are physiological in the liver of the newborn, and still more so in the fetus because of the blood-making activity of the liver. (M. B. Schmidt, Saxer, Askanazy.) These cell groups have been variously interpreted; they may be lymphocytes as they appear in true small cell infiltration, or they may be blood cells, *i.e.*, newly formed, young nucleated blood corpuscles (Hecker) or physiological, proliferating, giant liver cells (Hutinel and Hudelo). Erdmann (lit.) however, thinks—probably correctly—that they are blood cells. For more details concern-

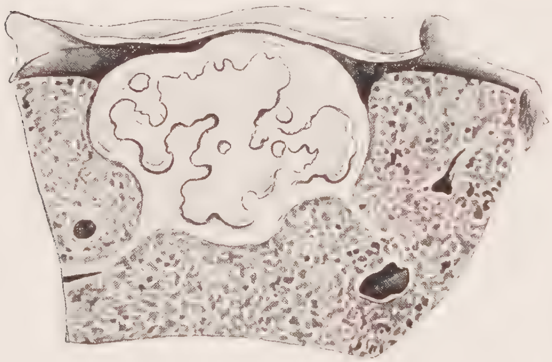


FIG. 453.—Large gumma of liver; map-like gummatous necrosis surrounded by a dense connective tissue capsule; perihepatic adhesions; markings of engorgement of liver; $\frac{4}{5}$ nat. size.

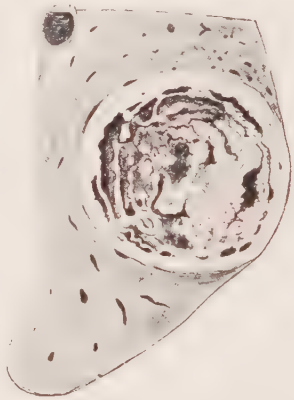


FIG. 454.—Globular gummatous tumor, centrally softened in the liver of a newborn; $\frac{4}{5}$ nat. size.

ing the hemopoietic foci of the liver which in intrauterine life are the main source of myeloid cells (after birth the bone marrow assumes this function), and which persist after birth in diseases of the fetus, see Wain and Lobenhoffer, Askanazy; comp. also under congenital universal hydrops, p. 241.

Polynuclear giant liver cells (fig. 452) often occur in very large numbers in congenital syphilis (Binder, Oppenheimer). According to some, they are formed chiefly by confluence of liver cells, according to others, by proliferation of one cell. Menetrier and Bubens Duval believe in both origins. They may be viewed as an attempt at regeneration without arriving at cell division. They have nothing in common with syphilitic tissue production; such pictures are frequent; the author found them in 50% of all cases. Zonicer believes that giant cells may also arise from the bile channels.

Diffuse interstitial hepatitis may go hand in hand with syphilis of the spleen, pancreas, lungs, bones, also with ascites, but rarely with icterus.

(*b*) **Gummatous Growths.**—Many of the so-called miliary gummata which have been described are probably nothing else than cell infiltrations, as mentioned above, present in non-syphilitic foci and in the newborn also (see Hochsinger, Lubarsch). But in other cases, the smooth section surface shows gray or yellow, irregularly shaped spots or opaque granules, or only microscopic foci of polymorphous cells which are miliary granulomas. Their centers are more or less necrotic, homogeneous and loaded with nuclear fragments. If these miliary gummas consist of necrotic masses with nuclear debris, poorly circumscribed, and situated in the indurated granulation tissue they are also called miliary necroses, when their derivation as granuloma nodules cannot be recognized (see v. Werdt); see fig. 455. This suggests a pure non-inflammatory toxic action (see Hueter); and since the interstitium of the liver is also altered in such cases, the miliary gummas are probably only an expression of intensive spirochetal action from collections of the organisms. (See Schridde and Schneider.) Large globular gummas are unusual. They may be mistaken for tumors (see Sauage and Gery) (fig. 454).

A peculiar picture results if the gummatous new growth extends from the hilum into the periportal connective tissue and infiltrates and narrows or encloses the portal vein or bile ducts (fig. 456). It then consists of spindling, branching, bacony white strands which may show yellowish, caseous, elastic inclusions here and there; they enter the liver parenchyma like rays, with or without interruptions, and may be modified to diffuse bacony infiltrations in the grass green liver tissue. The author observed this phenomenon in a 10 day old female child, 42 cm. long, icteric for 3 days (see Beck, Chiari, Sugi). Isolated bile channels may resemble the vas deferens on account of thickening of the walls and narrowing of the lumen. Icterus may be absent; in other cases, the liver is grass green. This is spoken of as peripyelophlebitis and gummatous pericholangitis. Microscopically, branches of the portal vein and bile ducts are found markedly thickened by spindle cell tissue; sometimes the ducts are especially so. The arteries often show thickening of the walls (fig. III, p. 464), and other diffuse interstitial changes are always present. (For condition of the umbilical vein, see under umbilical cord.)

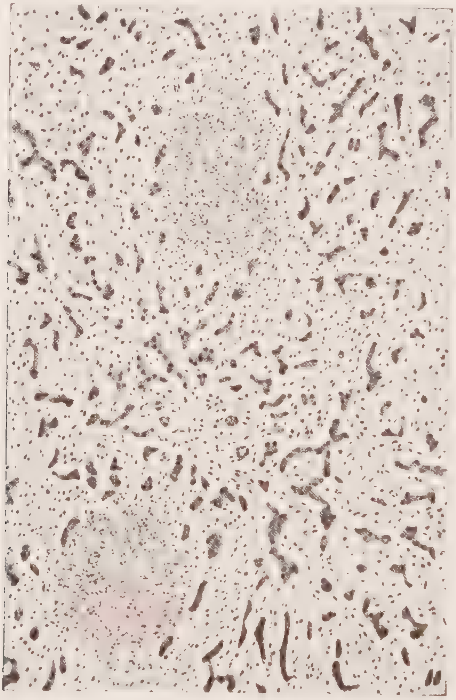


FIG. 455.—Miliary gummas (so-called miliary necroses) of liver in congenital lues. The foci, which consist of necrotic cell material with scattered nuclear fragments are poorly differentiated from the diffuse interstitial connective tissue proliferation; a few lymphocytes at periphery; (medium magn.).

In the later manifestations of congenital syphilis, the liver affections correspond partly to those of acquired syphilis. Large nodular or lobulated livers may develop directly from the congenital form from the strand-like connectiye tissue proliferation. Marchand supposes that the diffuse connective tissue hyperplasia may be the starting point of a typical hypertrophic cirrhosis (comp. sub a). Orth mentions gummatous pericholangitis in a 19 year old girl with late congenital lues (see also Dutsch).

Acquired syphilis in adults shows various forms.

(*a*) From focal proliferation of interstitial connective tissue there form septa of young connective tissue often very broad, starting from the periphery and penetrating into the interior. With the subsequent change into scar tissue contraction takes place, pulling the surface inward and dividing it into large lobes which may sometimes be palpated as tuberosities through the abdominal wall and be mistaken for tumors. In this way the lobulated liver is formed (hepar lobatum), which is very irregular as if it were tied up in various directions with strings. The most and deepest indentations, as a rule, are in the vicinity of the suspensory ligament (fig. 457). The capsule is thickened and usually shows numerous tape and thread-like adhesions with the neighborhood, especially the diaphragm (fibrous adhesive perihepatitis). The lobulated liver, although in the beginning somewhat enlarged, may finally contract to the size of a fist.

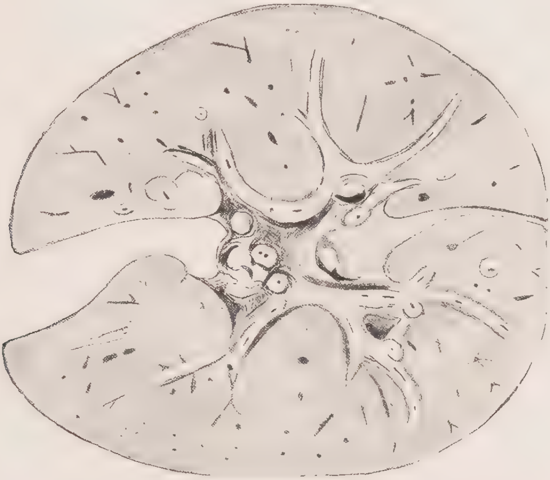


FIG. 456.—Pericholangitis and peripylephlebitis gummatous in flint liver; organ is cut through; newborn, 5 days old; body length 41 cm.; spleen 15 gms.; no icterus; 7/8 nat. size.

Part of the liver parenchyma atrophies, first where the broad septa become established, and then from the constriction (pressure atrophy). Often the rest of the parenchyma undergoes compensatory hypertrophy in the form of coarse lobules, and in this way the dense globular form of the lobes is brought about (see Melchior).

Generally speaking, interstitial hepatitis leading to lobulated liver is characteristic of lues, and this view gains in certainty if the fibrous strands or other parts of the liver contain gummas. There are, however, forms of interstitial syphilitic hepatitis which correspond to a coarse granular cirrhosis; they sometimes originate from congenital syphilis and may be combined with considerable enlargement of the liver due to vicarious proliferation. Cases are also seen in which only a part of the liver has undergone these changes. A considerable splenic tumor may be present (comp. weights, p. 224), but there is no icterus. Such lobulated livers may show amyloid degeneration, when the tuberosities become especially thickened and elastic (palpable through the abdominal wall), and frequently the whole organ becomes elongated. These tuberosities have been known to enter a hernial sac.

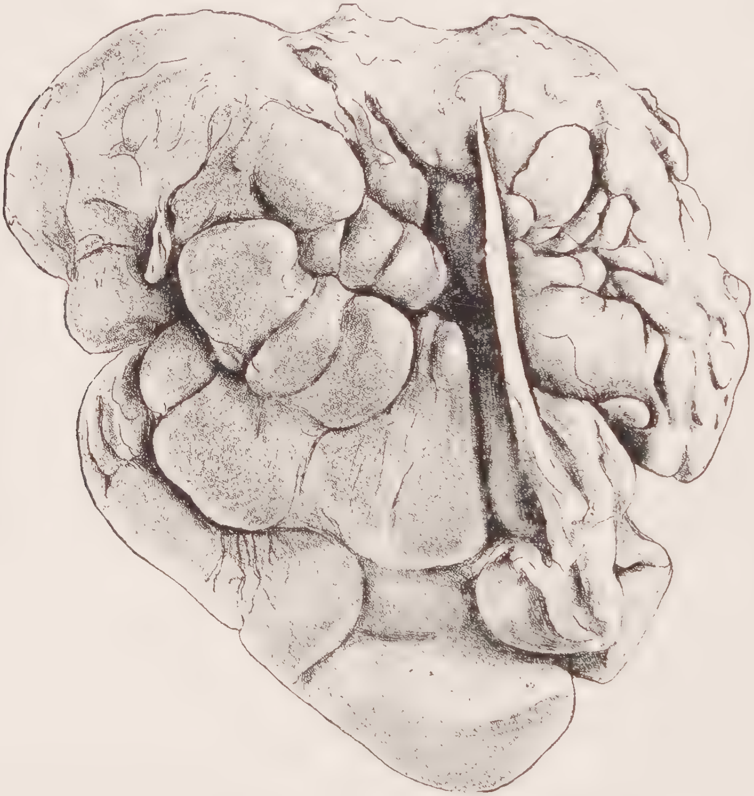


FIG. 457.—Lobate liver with adhesive fibrous perihepatitis, from a syphilitic man; ½ nat. size.

(*b*) **Gummatous Nodules.** The edges of these circumscribed inflammatory new structures usually terminate in acute angles with angular indentations in their contours. They are pale yellow, cohesive, dry, cheesy, of firm consistency, difficult to indent with the finger nail, and are often surrounded by glassy connective tissue (fig. 453). They are found singly or multiple, and of the size of peas, cherries or even fists, frequently in the depth of a cicatricial constriction of the surface which is often adherent to the adjacent organs, (adhesive perihepatitis). Occasionally they are deep in the liver tissue, more frequently in the vicinity of the suspensory ligament, at the lower margin of the liver, or around the hilum. Sometimes they appear like true tumors, *e.g.*, carcinoma metastases, in the midst of unchanged liver tissue, or in rare cases prominently globular on the surface just as sarcoma or carcinoma nodules. They have often been mistaken for these on palpation through the abdominal wall as the author observed, *e.g.*, in the case, fig. 458, in which the localization is especially striking alongside the suspensory ligament, always exposed to physiological lesions and pull (mentioned, p. 261 under gummas of lymph nodes) (surg. lit. by Konig). But usually a yellow center is differentiated from a gray, glassy periphery, although quite homogeneous, cheesy gummatous, pale yellow nodules may be found which stand out in the normal, soft, macroscopically unchanged tissue of the section surface. Such cases have even been operated (comp. Cumston, lit.).

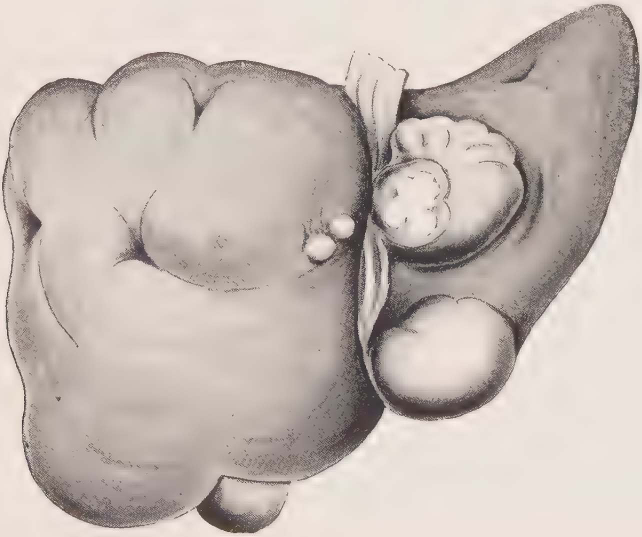


FIG. 458.—Four nodular projecting gummas of the slightly lobate liver of a' woman 52, grouped near the suspensory ligament, clinically diagnosed carcinoma. The largest mass (6.5 cm. × 5.7 broad × 5.7 thick) is cut fontally showing clover leaf-like necrotic (caseous) projecting material surrounded by gray, glassy tissue. Below, the gall bladder extends over the liver margin; ⅔ nat. size.

Recent gummas are grayish red and fairly soft, but with increasing necrosis and fatty degeneration the characteristic changes mentioned develop, at times with the addition of cicatricial changes. They may even be absorbed or be changed to scar tissue. Frequently, scar-like fibrous tissue radiates from the vicinity of gummas into the liver substance causing contractions.

(*c*) A combination of gumma with lobulated liver is frequent, and in the fibrous strands are yellow and gummatous inclusions markedly projecting. The liver is lobulated and often extraordinarily small, since the marked cicatricial contraction causes atrophy.

Differentiation between Gummata and Tubercles. The dryness, yellow, cheesy condition, marked elastic firmness and glassy cicatricial connective tissue coating usually permit of sharp differentiation from the caseous tuberculous nodules and likewise from tumors such as sarcomas and scirrhous carcinomas.

(Lit. syphilis of liver by Herxheimer E. XI, 1907, congenital, E. XII, 1908, clinical and lit. by W. Ebstein in textbook of sexual diseases by Finger, Jadassohn, etc., Vienna, Holder, 1912.)

Actinomycosis.—This is infrequent in the liver and when found, has usually arisen by continuity from the vicinity, peritoneum, retroperitoneal tissue or pleura-diaphragm, and thus there is only one, or at most a few foci. Occasionally isolated or even numerous disseminated metastatic nodules appear in the interior. The foci are yellow, soft, fibrillar, meshy, or honeycombed and saturated with pus. They are peculiar looking abscesses reaching at times the size of a walnut, or small apple, to that of a child's head and more, usually from confluence.

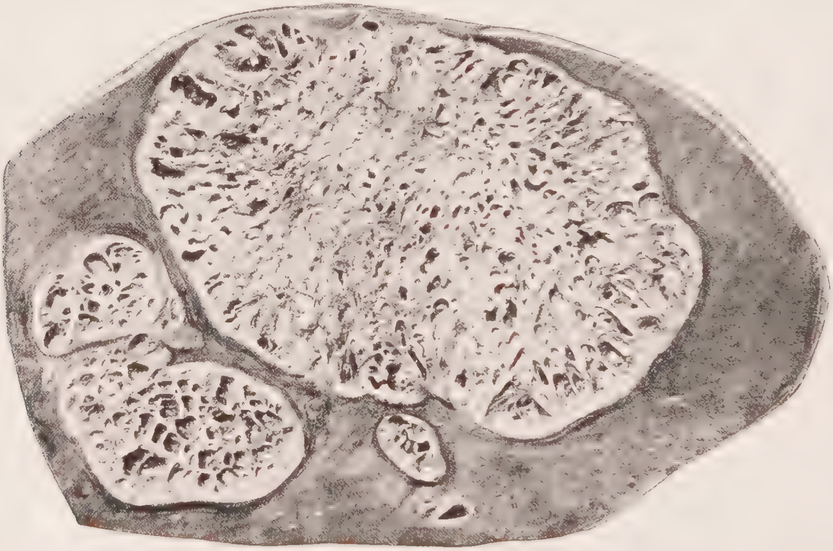


FIG. 459.—Actinomycosis of liver, several honeycomb-like abscess nodules; partial washing out of pus makes the dividing walls and honeycombs plainer. Piece of right lobe with frontal section of the case mentioned in text of a servant 19 years old; ½ nat. size.

A preparation in Basel from a 19 year old girl, farm servant, shows two masses almost the size of fists and some smaller, rounded, honeycombed to loculated, and filled with viscid pus of intensive yellow color containing many granules. The septa in the cavity are white after washing away the pus. Weight of the liver is 2750 gms., capsule is thickened, villous, attached to the diaphragm, which is marbled with yellow striae and fistulae; the right pleura is similarly marked and is firmly attached to the lung by thick scar tissue. The lung contains some abscesses approximately the size of walnuts; there is a fistula between the umbilicus and xiphoid process, weight of spleen 453 gms.; duration of illness 9 months, with the picture of empyema of the pleura, rupture into the liver and the formation of fistulae; portal of entrance, probably lung.

Actinomycosis of the liver is usually secondary to intestinal actinomycosis, either by continuity in the retroperitoneal tissue, or by invasion through the portal vein. Entrance through the artery is very rare, *e.g.*, in the case of Moodie starting with actinomycosis of the superior maxilla.

A primary actinomycosis of the liver is possible when spores reach blood and lymph vessels through the skin and mucous membranes and localize in the liver. Most observers doubt such occurrences, however, since an initial old pulmonary or intestinal focus may be overlooked or be healed without leaving trace (lit. to 1903 by Auvray: see Diehl, Seenger, Roth).

Glanders has been found in rare cases in the form of nodules in the liver (histology, p. 298).

Leprosy.—Tubercle-like nodules with giant cells may occur, but they have no general importance.

Lymphogranulomatosis (p. 267).—Occasionally numerous nodules and masses appear resembling tubercles or carcinoma. A very rare extensive cicatricial change was observed by Weis and Eug. Fraenkel.

Lymphomas and Leucocytomas (Leukemic Infiltration) (Appendix: Necrotic Foci)

In leukemic infiltration, the accumulation of lymphoid or myeloid cells is frequently so abundant that the organ attains an enormous size with a weight of 8 to 10 kilos. The consistency is fairly soft with the section surface reddish gray to yellow; in myeloid liver it is reddish brown and firm; the author has seen green periportal infiltrations in myeloid chloroleukemia. The lobular etching is erased, (myeloid leukemia) or is more prominent on account of white reticulated spots corresponding to the peripheries (chronic lymphatic leukemia). Sometimes grayish white strands of considerable width follow the branchings of the portal vein. Occasionally the individual liver lobules, the cells of which may be well preserved, seem to be remarkably swollen and larger than normal. To this picture which corresponds to diffuse leucocytic infiltration, more or less sharply circumscribed, small nodules, white to whitish red, may be added, or rounded, grayish white or grayish yellow masses, to the size of peas and larger. Microscopically, in lymphatic leukemia interacinar lymphomas, often nodular and sharply circumscribed, rounded or confluent, are seen, frequently in large numbers. They are heaps of compactly placed lymphocytes in a quite delicate reticulum in the periportal tissue, especially in the triangular fields, and the capillary system is filled with small lymphocytes. In myeloid leukemia, the infiltration is diffuse, intraacinar, pericapillary; the capillaries are filled with myelocytes, which may be so numerous that the liver cell columns are narrowed or even crushed. Complex arrangements, or rounded heaps, or nodules composed of cells and reticular ground tissue (myeloid tissue) are rare. Striae are much more frequent and these are predominantly intraacinar (occasionally periportal).

The same picture may be met in pseudoleukemia (aleukemia). In lymphogranulomatosis (see p. 945) white nodules in the liver simulate metastatic tumor nodules or even conglomerate tubercles. They begin in the periportal tissue and displace and penetrate lobules. The author has seen the picture of cirrhosis produced by marked connective tissue growth (rare). Small leucocytomas, the so-called lymphomas, are found frequently in typhoid fever, diphtheria, scarlet fever, measles, at times in other infectious diseases. (See M. B. Schmidt—hemopoietic foci, see p. 939.)

In the most varied infectious diseases (diphtheria, scarlet fever, etc., and especially in typhoid fever) microscopic necrotic foci are often found, usually in the center of lobules (see also McCrae and Klotz). These may be complicated by hemorrhages and cell infiltrations. The causative factors are toxins, or capillary occlusion by bacteria, fibrin thrombi, carried in phagocytes, *e.g.*, splenic endothelium, endothelium from intestinal blood vessels, or even capillary endothelium from the liver itself (Flexner, Mallory). See Gaffky, Engelhardt, Posselt, lit. in reference to the rare finding of typhoid bacilli in these foci. Faber believes the typhoid necroses are regular and specific findings in this disease, and consist chiefly of histiocytes which proliferate and immigrate at the point of the liver cell necroses, while lymphocytes and leucocytes are minor participants. Typhoid nodules are found also in the spleen and bone marrow. Minute liver necroses are also found in eclampsia, obstructive jaundice and severe intestinal diseases. The author saw a case of the latter type in a 2 months old boy with chronic gastroenteritis. The brownish red liver was thickly peppered with dots, from microscopic to macroscopic size, cloudy greenish yellow and in large numbers (alimentary intoxication or intestinal infection?). (See Amsler, Schneider, lit.) Chloroform also causes central necrosis, (Hildebrandt, lit.); Heinrichsdorff, lit. described the same condition in hyperemesis gravidarum, and Da Rocha Lima described necrosis of the intermediary zone in typhus.

Amyloid Liver (Bacony Liver)

Interstitial amyloid infiltration (so-called amyloid degeneration) develops as a secondary disease in all severe nutritional disturbances which cause anemia and cachexia. Among such diseases may be mentioned: tuberculosis, chronic suppurations especially those which involve bones, joints, lungs, etc.; syphilis, malaria, chronic renal disease, leukemia, pyelitis, cystitis, cachexia due to tumors, *e.g.*, suppurating carcinomas of the uterus. Cell destruction is the essential factor in amyloidosis.

It is assumed that under the influence of the diseases named, especially chronic suppuration, amyloidosis is due to a special protein body in colloidal solution, circulating in the organism, which instead of being eliminated, is precipitated out by the action of ethyl sulphuric acid and accumulates in certain organs, *i.e.*, in certain types of tissue, (*e.g.*, the blood vessel connective tissue apparatus). Thus, as a colloidal body, it is transformed from the sol into the gel condition (see Leupold).

Amyloid liver may develop alone but more often in company with amyloidosis of other, sometimes almost all, organs. It is especially common in the spleen, kidneys, intestinal mucosa, adrenals, lymph nodes, etc.

Microscopic Appearance.—The deposit, *i.e.*, formation of amyloid substance in the blood vessel connective tissue apparatus, leads to secondary pressure atrophy and degeneration of liver tissue. Usually the small intralobular arteries are involved first, and amyloid is deposited between the fibres of the media. The glassy substance is then found in the vicinity of the intralobular capillaries deposited in clumps and masses (fig. 460). It pushes between the endothelial tubes of the capillaries and the liver cells in that situation where some authors suppose there exist preformed lymph spaces, while others believe there is only a meshwork of lattice fibres (see p. 886). By compression, the lumen, which remains intact as to its endothelium, is more and more narrowed and finally occluded, while the liver cell scaffolding atrophies from pressure and is eventually changed into small brown masses (pigment atrophy). To a less degree it also undergoes albuminous and fatty degeneration. The liver cells themselves never show amyloid in their cytoplasm. Wherever they are destroyed, amyloid masses usurp their place and nothing but amyloid is found between the remains of the lobules. The central vein also undergoes the same change. Sometimes it is found chiefly in the interlobular portal branches but this cannot be recognized macroscopically. Again it may be first localized in the periphery, but, perhaps more frequently in the middle zones when the untouched peripheral parts show fat infiltration. The infiltration then progresses from the middle zone into both the peripheral and the central portions.

At times an extremely irregular distribution is seen, and heavy amyloid areas stand out almost like foci from non- or slightly infiltrated parts.

Amyloid gives macro- and microscopic reactions.

With iodine potassium iodide solutions (1 part iodine, 3 parts KI, 100 parts water), it gives a mahogany color, (tissues yellow); when treated afterwards with a solution of H_2SO_4 the amyloid turns dirty green to blue, according to the strength of the solution (10% is best). The reaction is quite plain.

Treated with methyl-violet (1:100), and washed in 1% acetic acid, the amyloid stains red; the tissue shows violet nuclear stain. This reaction is visible only in microscopic sections; moreover it is not reliable, since non-amyloid parts also show the resulting metachromasia. A beautiful microscopic effect, although not characteristic, is obtained with the double stains, hematoxylin and eosin; the latter stains amyloid red. The van Gieson stain gives brown nuclei and pale yellow amyloid substance.

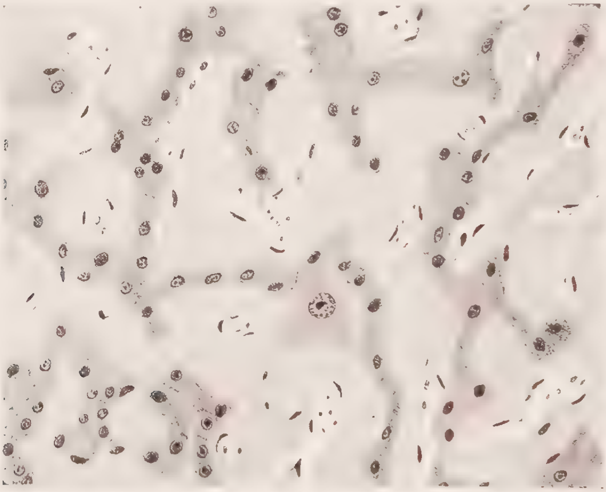


Fig. 460.—Amyloid infiltration of liver. Amyloid substance (light gray) between liver cell columns and capillaries, the latter in many instances much narrowed. Liver cell columns displaced and partly atrophic from pressure (med. magn.).

Macroscopic.—Slight degrees manifest no macroscopic changes. In more marked infiltration, the liver is enlarged, or if not enlarged, is at least heavier and firmer than normal. The specific gravity is increased in contradistinction to fat infiltration. In rare cases the liver may weigh up to 7 kgs. (normally 1.5–2 kgs.). The edges are rounded and blunt, the surface is smooth, the consistency dense, rigid and non-elastic. It cuts like smoked ham. The section surface is homogeneous, translucent; fairly thick slices are transparent, as if cleared in glycerin. The color is dark brown red, or pale grayish brown, or resembles boiled bacon and is waxy and dry. The paleness is due to the compression or crushing of numerous capillaries, while the brown color is due to atrophy of the liver cells; brownish red livers still contain blood. If the Lugol's solution is applied to the section surface and is washed off with water after a few seconds, the amyloid areas, previously pale gray now appear mahogany or chestnut brown in color; the non-amyloid areas are yellow, and sometimes the predominant participation of the middle zones may be recognized even macroscopically. In mild degrees, the proof is possible microscopically or macroscopically only by immersing a thin section in the iodine solution, and after washing, examining against a white background. As a rule, the whole organ is diseased, although not uniformly in all portions. Liver amyloid in circumscribed nodules is rare.

Fat infiltration is often coexistent, and then yellow, cloudy, opaque and gray or grayish brown transparent areas alternate with each other. Sometimes the central zones may appear green from bile pigments. Syphilitic hepatitis may be combined with amyloid in some livers, and has been observed even in children.

Glycogen Infiltration in Diabetes

In diabetes mellitus, abundant glycogen is usually present (see under pancreas). The organ in its earlier stages is often large, relatively heavy, has a peculiar rosy tint and a sort of transparency. In old severe cases, it is, as a rule, diminished in size and free from glycogen. Glycogen is a carbohydrate easily changed to grape sugar and is deposited either in solution or as hyalin clumps, drops or granules in the liver cells (fig. 436-f). First it is bound to the granules, then to the rest of the cell plasma as well as within the nucleus which is poor in chromatin and highly vesicular (Ehrlich, Meixner, Askanazy, Huebschmann, Rosenberg, lit.; Karamitsas, Klestadt, Scherflin, lit.). The cells are almost always hypertrophic with their protoplasm devoid of glycogen (Huebschmann). Finally, glycogen is deposited in the delicate lymph vessel network woven around the capillaries and columns of liver cells. Some believe, however, that extracellular glycogen deposition is a post mortem condition (Sjovall, Miyauchi). If abundant it is usually evenly divided, if moderate, it collects in the periphery of the lobules (Miyauchi). Rossle calls attention to the intensive fat deposits within the stellate cells and the formation of pericapillary collagenous bands from lattice fibers (p. 886). Glycogen appears under normal conditions in many tissues of the embryo, but also in adults in the liver where it is metabolized, (see E. Pfluger in reference to the apparatus regulating the sugar content of the blood under normal conditions, the antidiastase of the pancreas). Glycogen can be found in cartilage, muscle, leucocytes, bundle of His, embryonic membranes, endometrium (Wegelin), in pathological growths, *i.e.*, in various tumors, especially the congenital types, *e.g.*, rhabdomyoma, tumors of the testes, uterus, chorionic epithelium, adrenals, etc. In diabetes, glycogen is found in other organs such as the kidneys and myocardium.

Meixner thought he could establish an important relationship between the form of death and the quantity and distribution of glycogen for forensic purposes, so that, *e.g.*, an abundance of glycogen in the liver cells indicates sudden death while its removal into capillaries and lymph vessels (which is probably a post mortem condition—see above) or its complete absence points to a preceding agony, but Sjovall and Miyauchi have not verified this idea.

See Tomiselli (lit.) in reference to disappearance of glycogen after ligation of the common duct.

Demonstration.—Glycogen stains brown to wine red with iodine. Since glycogen (in contradistinction to amyloid) is readily soluble in water and very unstable, the post mortem preparation must be fresh on account of post mortem fermentative decomposition of glycogen into invisible grape sugar, and the sections must not come in contact with water which dissolves it. Sections either fresh, or better still, hardened in absolute alcohol, are placed in a thick solution of iodine and gum arabic (Ehrlich), or in iodine glycerin (Barfurth). The granules and droplets turn brown. Langhans advises the following technique: harden in alcohol, cut, place sections in a mixture of official tincture of iodine 1 part, absolute alcohol 4 parts, clear with oil of origanum, examine.

According to Gierke (lit.) and Arnold (lit.) the best method of demonstrating glycogen by stains is that of Best; fixation in absolute alcohol, then ammonia-carmine. (Glycogen red, nuclei blue, after previous hematoxylin staining.) See Neukirch, Rosenberg.

Pathological Pigmentation

(*a*) Brown or yellow pigment in atrophic liver cells as found in brown and cyanotic atrophy and other conditions due to constriction in cirrhosis, pressure by tumors or amyloid infiltration is probably in part derived from the blood since the atrophic cells are unable to elaborate the blood pigment into bile pigment. But it is supposed to be formed in part by the protoplasm itself, and to remain as a pigmented catabolic product (atrophic pigment infiltration). It gives no iron reaction, but belongs to the lipofuscins, since it stains with sudan. In reference to catabolic pigments, see p. 49.

(*b*) If granular blood pigment from the disintegration of erythrocytes, or any other pigmented bodies of whatever derivation, is transported in cells into the liver, it is deposited in the capillaries of the periportal connective tissue and in the peripheries of the lobules, in the cells of the sheath of Glisson, in the Kupffer cells, in vessel endothelium, and finally in the liver cells themselves. Some remains in the capillaries. The color of blood pigment varies between yellow, red, brown, and black. The iron-containing granules (hemosiderin) give the iron reaction (p. 372), a condition spoken of as siderosis (Quincke) or hemosiderosis. The Kupffer stellate cells, which are, however, often wing shaped (Reinke), were formerly defined as cells with projections, located between the capillary wall and the liver cells and clinging to both. Later their discoverer described them as belonging to the syncytium-like endothelium of portal capillaries. They are phagocytic to a high degree not only in relation to dead foreign bodies, but to erythrocytes and fat (pp. 891, 905, 950) and especially bacteria, (dead tubercle bacilli, etc.) which appear in the stellate cells in varying short periods of time after entrance into the blood stream. They have, then, a protective function, similar to that of the leucocytes, (see Schilling, lit., Nathan, Gilbert and Jomier). They are also an important link in the so-called reticulo-endothelial apparatus (p. 219); they help splenic function and substitute for it after splenectomy. In animals it has been observed that cinnabar, carmine, etc., injected into the blood are deposited in the liver, by preference in the stellate cells (see also spleen p. 221, and bone marrow p. 290). They play an important role in the regulation of cholesterin metabolism; if the liver cholesterin increases, the stellate cells accumulate lipoids (see Rothschild).

This pigment deposit is seen after absorption of disintegrated blood from stomach or intestine after hemorrhages, in cirrhosis, etc. Pigment infiltration after the melanemia of malaria is especially marked (p. 208), and is never in the gland cells, but in the endothelium and stellate cells. The parasites are also engulfed, because next to the spleen, the liver is considered the chief organ for their destruction (see Helly). Macrophages in the lumen and in the vicinity of capillaries also contain pigment. The pigment is later located especially in the periphery of the lobules and in Glisson's capsule; it does not give the iron reaction and disappears in liquor potassae (carbon pigment does not). The liver as a whole may swell and become dark green, or it may atrophy. (Details by Marchiafava and Bignami, see also Jansco.) Malarial pigment is doubly refracting (Schaudinn).

(*c*) In certain blood diseases in which an excessive amount of hemoglobin, either as erythrocytes or their fragments is brought to the liver, the organ may not be able to change the excess into bile pigment even if the cells are unimpaired. Deposits then occur in the liver cells and in Kupffer cells, partly as yellow, finely granular precipitates of iron-containing pigment (hemosiderin), or as red brown hemofuscin, or partly as colorless albuminates of iron diffusely present in the protoplasm of the cells. The granules in the protoplasm which collaborate in the iron metabolism are probably altered structural elements of the cells (plasmosomes) while the granules in the nuclei are modified kariosomes (see Gambaroff). In pernicious anemia and hemoglobinemia (p. 186) therefore, the liver is orange yellow or light brown or russet in color. In addition, in pernicious anemia it often undergoes central fatty degeneration (see p. 903). But the spleen and bone marrow are also storage depots for iron, although as emphasized by Lubarsch, there is no parallelism between the degree of blood destruction and iron accumulation in the tissues. (See Nishimura for combined ammonium sulphate and ferrocyanide hydrochloric acid method for microscopic proof of iron. He found iron in 97.3% of all livers.)

Rossle designates this form of iron liver, in contradistinction to the hemosiderotic (*b*) as hemochromatotic, because general or local hemochromatosis is coincidently present (p. 928).

(*d*) Pigmentation by bile gives the Gmelin color reaction with nitric and nitrous acids. This pigment infiltrates the cells diffusely or in granules. Details will be discussed under icterus (p. 1012).

(*e*) Sometimes anthracosis (coal deposits) is found (p. 421) in stellate cells around the central veins, in the perilobular tissue and often within small lymphoid foci. At times, grayish black dots are seen macroscopically under Glisson's capsule or on the section surface. The portal lymph nodes may be pitch black.

(*f*) Silver taken for some length of time as a therapeutic measure appears in various organs as fine black granules principally in the stellate cells and Glisson's capsule of the liver, kidneys, arterial walls, and especially in the skin (argyrosis, gray, dark color).

Reaction: after treatment with concentrated nitric acid the granules disappear, but reappear on the addition of ammonium sulphide.

(*g*) For details of the pigment derived from pigmented sarcomas and carried to the liver, see p. 958.

Appendix. Calcification is quite rare, and occurs mostly as the calcium carbonate and phosphates, rarely as calcium soaps, (Hagiwara, Bendelhuber) usually in centrally necrosed lobules; it has, however, been observed in Glisson's capsule in nephritis (see Babes, Liebscher, Hedinger, Rollet, Ceelen).

Tumors of the Liver and the Small Bile Channels

BENIGN TUMORS

Cavernous Angiomas of the Liver (Cavernomas).—These are usually found accidentally, most frequently in older individuals, occasionally, in the newborn, when their appearance differs slightly. In a newborn child, the author observed a lumpy, thickened grayish white area in the middle of the right lobe into which coursed a large number of injected vessels. Section revealed a well circumscribed tumor 2 cm. broad by 1 cm. deep, partly brown red and cavernous and partly lighter white red and solid (see lit. by Michailow).

The more usual type reaches to the surface where it appears dark blue red, and of the size of a cherry to a walnut. These tumors are sometimes multiple and perhaps do not give the impression of tumor, especially if fairly large. As a rule, the liver is not enlarged except in cases in which the tumor reaches the size of a man's head. Trauma to the abdomen may cause rupture and hemorrhage.

On sectioning, angiomas collapse and discharge quantities of dark red (venous) blood. If this is washed away, a delicate meshwork is seen which either blends diffusely with the adjacent tissue, or, in the larger cavernomas, is circumscribed by a sort of capsule.

Microscopically, we see wide meshes lined with endothelium. The cavernoma is often confined by a connective tissue boundary and fragments of liver cell scaffolding may be enclosed in this border zone.

Thrombosis is common within the meshes, and organization starting from the proliferating meshes ends in fibrous changes which cause the angiomas to atrophy, become less vascular or completely avascular, grayish red, or grayish white, and sometimes fleshy and tough like a fibroma. In addition to this organization of thrombi and thickening of septa, Merkel demonstrated a direct narrowing of the blood spaces by the development of subendothelial striated connective tissue layers, (see also Kasai). The thrombi and scaffolding may calcify.

It was formerly assumed that the origin was in a capillary ectasia with primary or secondary atrophy of liver cells to which was added secondary proliferative processes in the vessel walls in the vicinity, and in the interstitial tissue. This conception is now displaced by other theories, some of which assume there is a true new formation of vessels induced by invasion of connective tissue, as was thought by Virchow, or a tissue malformation. The latter is defined by Ribbert and Bruchanow as a separate embryonic fragment of a small vessel anlage which could not enter into normal relation with the liver cells (see also Roggenbau, who describes two "carcinomas" which he thought to be true tumors arising from the hepatic venous system). Pilliet called them fetal inclusions, Schmieden, local tissue malformations leading to an excessive production of vessel connective tissue as compared to the epithelial elements, but not true new formations. Today, they are frequently called "hamartomas" which means faults in tissue combination, faulty blending of tissue (from the Greek, E. Albrecht). There are cases, however, in which these hamartomas develop into autonomous true tumors (hamartoblastoma), although this is the exception, and these tumors often quite large, or small and innumerable, occasionally are associated with angiomas of the skin (Roggenbau), and as in Ribbert's case, with a cavernoma of the spinal column. At any rate, it can not be said that acquired capillarectasy is unable to give rise to hepatic angiomas, because there are cases of multiple cavernomas in advanced age, without increase of volume which give a pronounced impression of ectasia and which show plain transitions into capillaries of the portal vein. In the disseminated telangiectasia of the liver so common in cattle, many authors assume that congestion, focal necrosis of liver cells from atrophy, fatty degeneration or necrosis, are all important as primary factors. But Joest (exhaustive lit.) does not accept these explanations and considers them capillary ectasias, as well as cavernomas, in a narrower sense, malformations. (Details by Joest.)

Nodular Hyperplasias and Adenomas.—Nodular hyperplasias occur as compensatory proliferations after destruction of liver tissue, especially in cirrhosis (see Kretz) and also after cell destruction in sepsis, poisoning, etc., (Yamasaki). The areas jut out on the section surface, and are, apart from those in cirrhosis, not very sharply outlined from the normal tissues to whose architecture they adapt themselves without displacing it. Not rarely they are shaped like rosettes with a vein in the center. This will be met again in Wilson's disease, p. 970.

Adenomas can be differentiated into those springing from the liver cells and those having their origin in the bile channel epithelium. The former are rarely multiple and appear as light brownish, reddish or grayish white, smaller or larger tumors, often encapsulated and soft which may show macroscopically a texture of different design than the surroundings, *i.e.*, with an irregular, well-rounded lobular etching. The author, *e.g.*, saw three adenomas near the suspensory ligament in a 72 year old woman with a brown atrophic liver; two were of the size of chestnuts, the third as large as a pea. Microscopically, the adenomas imitate the lobular design of the liver, but with an irregular system of capillaries and convoluted liver cell scaffolding (liver cell adenomas). The larger cells often contain much fat and may secrete bile. The tumor compresses the adjacent liver tissue thus differing from hyperplasia. Multiple adenomas may put in their appearance in an otherwise unaltered liver, as seen by the author in a 46 year old woman with a nodule the size of an apple in the left lobe, and many small ones in the remainder of the liver. If they occur in cirrhosis, the separation from hyperplasia is difficult. Sometimes a single, firm, pale focus, or perhaps multiple nodules are found, consisting of thick tubules resembling bile channels (tubular bile duct adenoma). The connective tissue may be abundant between the tubes. Both forms of adenoma may occur in the same liver.

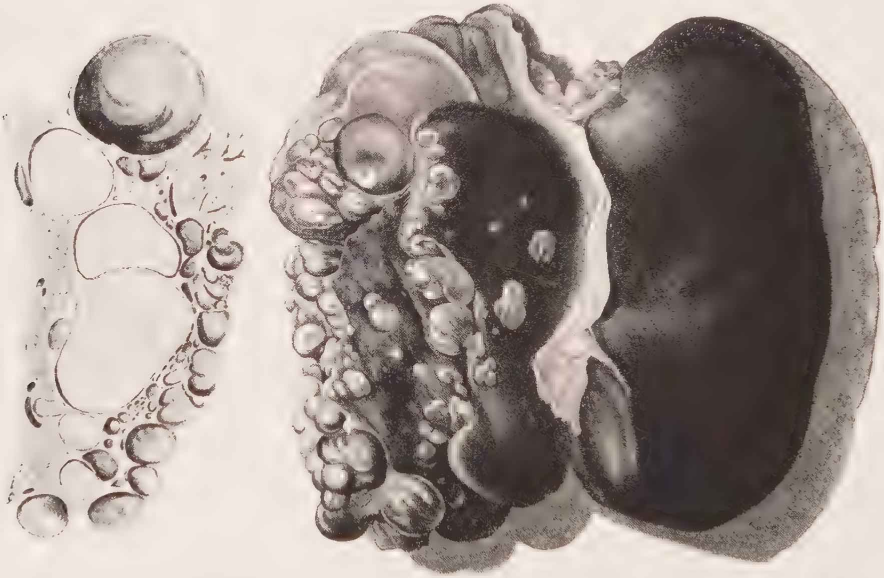
In a 21 mos. old girl, Hippel described a congenital mixed tumor which contained mostly adenoma tissue but also cartilage, keratosing pavement epithelium and pigment.

There are transitions from hyperplasia to adenoma and then to carcinoma, as well as directly from hyperplasia to carcinoma (see Grawitz). The bile duct adenomas may also become cystic by the retention of secretions, (cyst adenomas). As mentioned before, in cirrhosis of the liver of varying etiology, abundant bile duct proliferations and hyperplasias of liver cells appear. The border line toward adenomas is often difficult if not impossible to determine; the main evidence consists in displacement of adjoining tissue (see Dibbelt and Bartel; lit. in appendix).

Cysts of the Liver.—Only a small number are simple retention cysts caused by the secondary separation of preexisting, or newly formed bile channels. Retention cysts as small or smaller than a hazel nut sometimes are found in large numbers, as the author saw in an atrophic, slightly cirrhotic liver in which tiny cysts, filled with thick contents like bile, were scattered in countless numbers in the expansive interlobular connective tissue. The other type, serous cysts, are believed to be lymph cysts.

Most hepatic cysts are due to developmental disturbances in the intrahepatic bile channels. Most frequently they are isolated, small, subcapsular affairs filled with bile-like, slimy, or watery, clear, serous, or yellowish fluid; they are transparent, not prominent, and lined with ciliated or simple cylindrical epithelium, exceptionally, with pavement epithelium. They are supposed to be derived from primary snaring off of the vasa aberrentia of the bile channels, the mucous glands of which supply the secretion. More infrequently, there are found solitary cysts up to the size of a fist or larger, with one or several compartments, lined with ciliated cylindrical, or pavement epithelium. The wall may show stalactite-like projections which suggests the confluence of several cysts. These may be congenital, and have been known to impede labor (Witzel, lit. by Plenk, Konjetzny Sonntag). Cystic livers are rare; the organ may be enormously enlarged and filled with a many chambered system of thin, smooth-walled cavities filled with water clear liquid. They crush the parenchyma and bulge prominently as bluish translucent masses on the surface. The remaining intact parts of the liver often undergo compensatory hypertrophy. It is rarer to encounter cyst formation like bunches of grapes in the right lobe as in fig. 461, or as in Haberer's case, in the left lobe. Castelli saw multiple small cysts in the center of the liver with a poorly defined area consisting of a cavernous hemangioma.

The cystic liver is probably due to an embryonal developmental disturbance in the bile channel system, which prevents the union of single or many small bile ducts which develop from the liver cell scaffoldings with the larger ones which develop by continuous extension from the primary liver diverticulum, (Sabourin, v. Meyenburg, see also Broman). Others speak of multilocular adenocystomas, but there are no tumor-like proliferating processes of the epithelium (v. Meyenburg, lit., see C. Hofmann, Weishaupt, Mannsohn, Vorpahl, Berblinger). In the remaining tissue, between the cysts, broad fibrous strands push into the lobules and may contain many portal vein branchings, some occluded, with abundant bile channel proliferations. From the latter there are transitions to cysts. These cysts with blind ends are lined with cylindrical, cubical or flat epithelium. The previous communication with secreting liver parenchyma is soon lost, and with it the bile contents; they then contain epithelial secretion. In addition, obliteration of normal bile channels occurs (Sabourin, Muller, lit.). Cystic liver may be congenital, but most often is found in old people, and rarely in the young. It is often accompanied by cystic kidneys (illustr.).



FIGS. 461–462.—Cystic liver, cysts almost exclusively in r. lobe; compensatory hypertrophy of l. lobe of woman 71 years old. Left frontal section through part r. lobe; ⅓ nat. size.

The liver may become very heavy. In the collection of Basle is one of 7130 gms. from a woman 48 years old with coincident cystic kidneys. Weights of 10 kilos have been reported (Dmochowski and Janowski). Icterus and other symptoms of disturbed liver function are absent, but there may be congestion of the portal vein and the sequelae of ascites, splenic tumor, and gastrointestinal catarrh (Thole, lit.).

The true biliary system may soon lose its bile contents which are absorbed by the lymphatics, and it contains then a colorless fluid such as is seen in hydrops of the gall bladder (p. 999). This fluid is said to originate from the mucous glands, or epithelium undergoing mucoid changes in which case the fluid is slimy, or it is a serous epithelial secretion or watery transudate of the walls.

Malignant Tumors

Sarcomas.—Primary sarcomas are unusual, either as single or multiple nodules. There have been described: spindle and round cell sarcomas, hemorrhagic round cell sarcomas, (Bruck), giant cell angiosarcomas (Arnold, Crispell), some like chorion epitheliomas, (Marx, Nazari), hemangio-endotheliomas (Ravenna), malignant hemangio-endotheliomas (B. Fischer, see also Lohlein, Kahle, lit.), more rarely, pigmented sarcomas (melanotic perithelioma in a case of Nazari). In a 65 year old man, the author saw a spindle cell sarcoma as a large nodule sharply circumscribed from the liver tissue, polymorphocellular, partly myxomatous, partly necrotic. The liver weighed 5850 gms.; the spleen was swollen, no metastases. They may appear in children (v. Kahlden, Cesaris-Demel, Dionisi, Pepere, Borsowski, Holm, Carmichael and Wade, lit.; Theodorow, Bertelli, de Vecchi, Constantini, lit., Wilke, Hedren, Saltykow, Dubs, Terplan, lit.).

Sarcomas have been observed in cirrhosis (case of Kothny, lit.; Hachfeld, case of malignant endothelioma). Rolleston and Trevor describe a primary sarcoma in a cirrhotic liver; both carcinoma and sarcoma starting from parenchyma cells and connective tissue in a cirrhotic liver are described by Dominici and Merle.

Secondary sarcomas in their various forms appear frequently. The metastases of melanotic sarcoma looking like india ink splashes may be especially numerous, although the primary tumor, *e.g.*, of skin or eye (chorioidea) is often quite small. In the case of fig. 428, the liver weighed 8118 gms., and innumerable metastases were found in almost every organ. The eye had been removed one year before death. As a general rule, metastasis takes place early. But in a case of Ceelen, it occurred 7 years after the enucleation of the eye (see also Goldzieher, after 10 years).

The form is in round nodules like truffles sticking in the liver, or larger tumor infiltrations, white, brown, black or spotted, and on account of the regular extension into the vessels, a certain clumsy lobular radiating arrangement may be recognizable for a long time. Especially pronounced cases of this kind are called "melanotic radiating sarcomas." Nodules and infiltrations often combine, or there is a mixture of white, brown and black colors. The liver containing metastases of sarcoma may reach enormous size. Umbilication, as in carcinoma, is unusual, (comp. p. 966); indeed sarcoma nodules usually bulge as lumps or globules on the liver surface.

Extensive cystic metamorphosis of the nodules is by no means frequent, but in a man 55 years of age, the author saw tumor cysts the size of a child's head, some perfectly smooth-walled with sanguino-serous contents, in a liver weighing 10,900 gms. The primary growth was a sarcomatous myoma in the gastric cardia which ulcerated and proved fatal from hemorrhage.

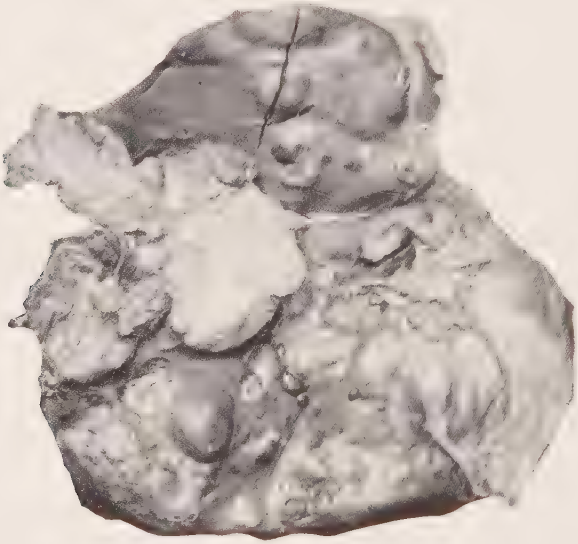


FIG. 463.—Metastatic melanosarcoma of the liver. View of the under surface showing numerous larger nodules. There were also innumerable smaller nodules. The primary tumor was in the retina. Patient died 6 months after removal of the eye. No difficulty is attached to this diagonosis because of the characteristic black colour of the nodules. L. H. #1810.

A single metastatic growth in the liver to the size of a man's head may be mistaken for a primary sarcoma as seen by the author when the primary growth was in the thyroid. The tumor cells spread via the blood circulation, they occlude the capillaries and grow from them into the parenchyma. The macroscopical black pigment, tumor-melanin, containing sulphur but no iron, is microscopically yellowish brown, and the pigment of disintegrated sarcomas, even those situated elsewhere, can be transported through the blood stream, somewhat like cinnabar, and be deposited in the liver, spleen, bone marrow, etc. In the liver it is found in the capillaries and interstitial tissue, in sufficient quantities to cause distinctive coloring macroscopically (see under pigment sarcoma of skin).

The bilateral tumors of the adrenal glands and its vicinity occurring in children in the form of malignant neuroblastomas of the sympathetics are not easily distinguished from a hemorrhagic, necrotic, round cell sarcoma, and often lead to enormous diffuse infiltration of the liver as well as of the bone marrow and prevertebral hepatic glands (see Landau).

Carcinoma of the Liver.—So-called primary carcinomas of the liver (*i.e.*, of liver cells and of the bile duct epithelium) are quite rare and of little practical importance. Several forms occur of these two main groups.

A massive tuberosity develops isolated, or with secondary nodules in the vicinity (massive cancer, Hanot). It may reach the size of a man's head. The author saw one (fig. 464) in the left lobe of an 83 year old man, almost as large as a child's head, nodular, with pseudo-fluctuation; on cross section, it presented a very colorful picture with alternating grayish red, grayish yellow, clay colored, brownish to yolk yellow, soft masses, penetrated here and there by white sinewy strands. Only a narrow edge remained of the left lobe. There was a plug as thick as a lead pencil in one of the branches of the portal vein. Microscopically, nests and columns of polymorphous cells were seen, some giant cells, some smaller, many with remarkably large or with multiple nuclei. These roughly granular cells which contained fat, were reminiscent as to their form, of angular liver cells. Hemorrhages and necroses had occurred in the tumor tissue and invasion of tumor cells into vessels and connective tissue. In a second case, in a man 40 years old, the right lobe contained a tumor larger than a fist; on section, it was pale yellow and dark red, there were many metastases in the lungs. Microscopically, there were large angular cells arranged in alveoli with bile pigment in larger masses between, and partly within the tumor cells. (See the case in a 33 year old man, p. 964.)

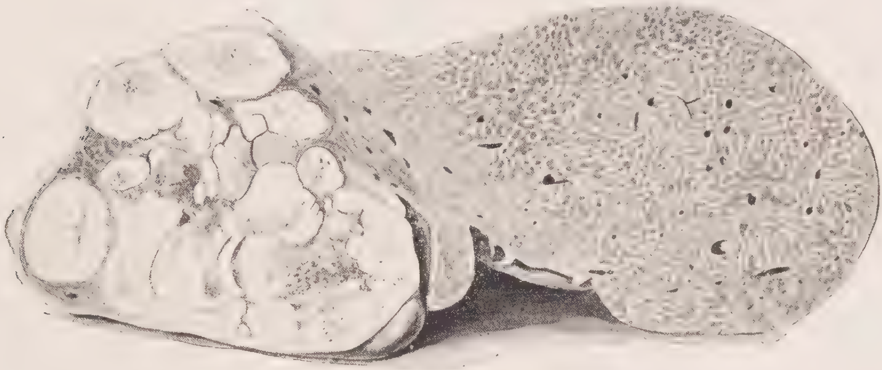


Fig. 464.—Nodular primary carcinoma of l. lobe of liver of man 83 years old. Horizontal section lower aspect (pict. f. orientation Fig. 465); ½ nat. size (microscopy, transition of type A to B; see text below).

In cirrhotic livers, (there are exceptions, however) there is (*a*) uniform invasion with multiple nodules (nodular cancer, Hanot) which are more or less sharply circumscribed and white, reddish or bile stained. Such a specimen gives at first the impression of metastatic nodules, but the umbilication is not pronounced. The second type is (*b*) a diffuse tumor infiltration, and the third type (*c*) is a combination of nodules and infiltration. This is spoken of as carcinomatous cirrhosis (cancer avec cirrhose, Hanot). Flat bosses and granules show prominently on the surface. There are transitions between these types.

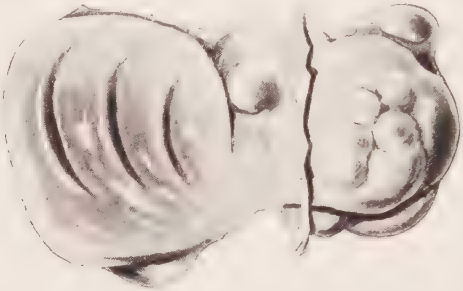


Fig. 465.—Primary large nodular carcinoma of liver, chiefly in l. lobe; deep transverse pressure furrow in both lobes; three parallel diaphragm furrows in right lobe; see Fig. 464.

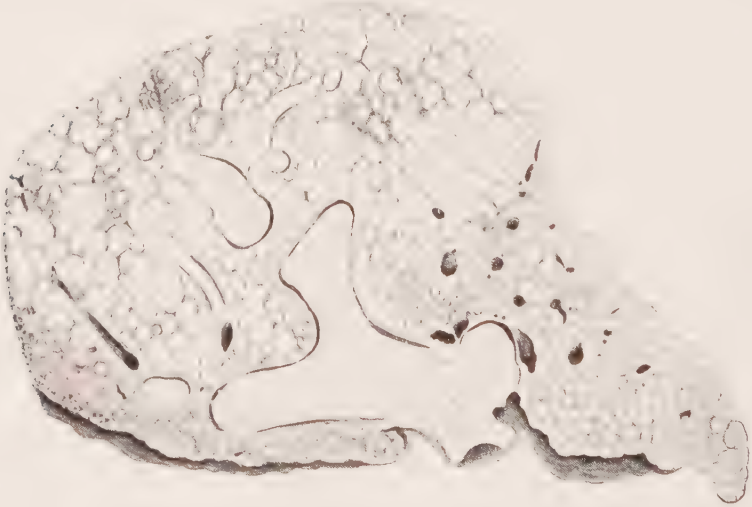


Fig. 466.—Primary carcinoma in a cirrhotic liver (horizontal sect.). Tumor plugs in the portal vein and its branches, also invasion into hepatic vein. The simple cirrhotic parts, not carcinomatous are to the right; 64 year old man with hemorrhag. ascites; spleen 12:8:4; Microsc: type B, see text, p. 961; ½ nat. size.

The liver may be considerably enlarged in either variety, but especially in (*b*) and weigh up to 10 kilos. It is firm to hard and often shows a thickened capsule. Sometimes, however, it is actually decreased in size and resembles externally an atrophic cirrhosis. This was seen by the author in a 64 year old man (fig. 466), with marked ascites, with multiple bile channel cysts on the liver surface and nodular liver tissue hyperplasia. Numerous greenish tumor plugs were found in veins, and in the branches of the pulmonary arteries, which is rare (see Wegelin, lit.). The cases of the second group give clinically the impression of cirrhosis combined with marked enlargement (with ascites).

Probably the liver cells themselves are the most frequent starting points of carcinoma (Schuppel, Siegenbeck van Heukelom, the author, Pollak-Daniels, Goldzieher and v. Bokay, lit.); some deny there can be a progressive growth by metamorphosis of liver cells into tumor cells (Ribbert and others, lit. by Wegelin), but the author as well as Goldzieher has seen pictures which can easily be interpreted in that sense. The bile channel epithelium may also be the starting point (lit. by Herxheimer, who found tubular forms with high cylindrical epithelium). B. Fischer would have us consider most adenocarcinomas of the liver as originating from the bile channels, but this is opposed by Wegelin for very good reasons. Besides this, tubular adenomas, and nodular hyperplasia such as the one of Tschistowitsch who reported a very interesting case of carcinoma of the liver originating in regenerative hyperplasia, may change into carcinomas. Indeed many so-called adenomas of the liver, especially the multiple ones, are really primary multiple carcinomas (see p. 954, lit. by Schmieden).

Microscopically, the author distinguishes two chief forms of carcinoma of the liver:

I. Liver cell carcinoma, carcinoma hepatocellulare, or so-called parenchymatous liver carcinoma (some call this hepatoma, a term not sharply defined and therefore inadvisable, because an adenoma of the liver might be called by that name with equal justification).

One type (*a*) carcinoma hepatocellulare solidum is composed of solid plugs, in alveolar arrangement surrounded by connective tissue; the plugs are made up of large cells, giant cells and smaller polygonal cells. This alveolar type is considered by many without due cause as the only true liver carcinoma. After clearing of the protoplasm the cells show a coarse granulation, enlargement of nuclei and increased abundance of chromatin, etc., which points to their transition from the type of liver cell.

The second type (*b*), much more common, is composed of columns and tubes surrounded by capillaries and delicate connective tissue fibrillae. The columns, a mixture of large and small cells, are of varying thickness, sometimes equal to the width of ten or twelve cells; they may be solid throughout, or partially or abundantly canalized by disintegration; the lumena, then, of unequal diameters, poorly circumscribed, as a rule, often contain large quantities of detritus-clumps and granules of bile, *i.e.*, of bile pigment. This is illustrated in fig. 467, taken from the work of Goldzieher and v. Bokay. There are also dainty tubular formations filled with bile, which resemble bile channel proliferations, but are, according to Goldzieher and v. Bokay, only pseudo-bile channels. The peripheral cells of the columns, *i.e.*, those which touch the capillaries may not differ from the rest, but sometimes they are of cylindrical shape. In places in which the solid plugs predominate there is a similarity to adenoma, but everything is more atypical, the cells are more polymorphous, there are many giant cells, and often a syncytium, with many nuclei or isolated giant nuclei. The tubular areas do not resemble adenomas;

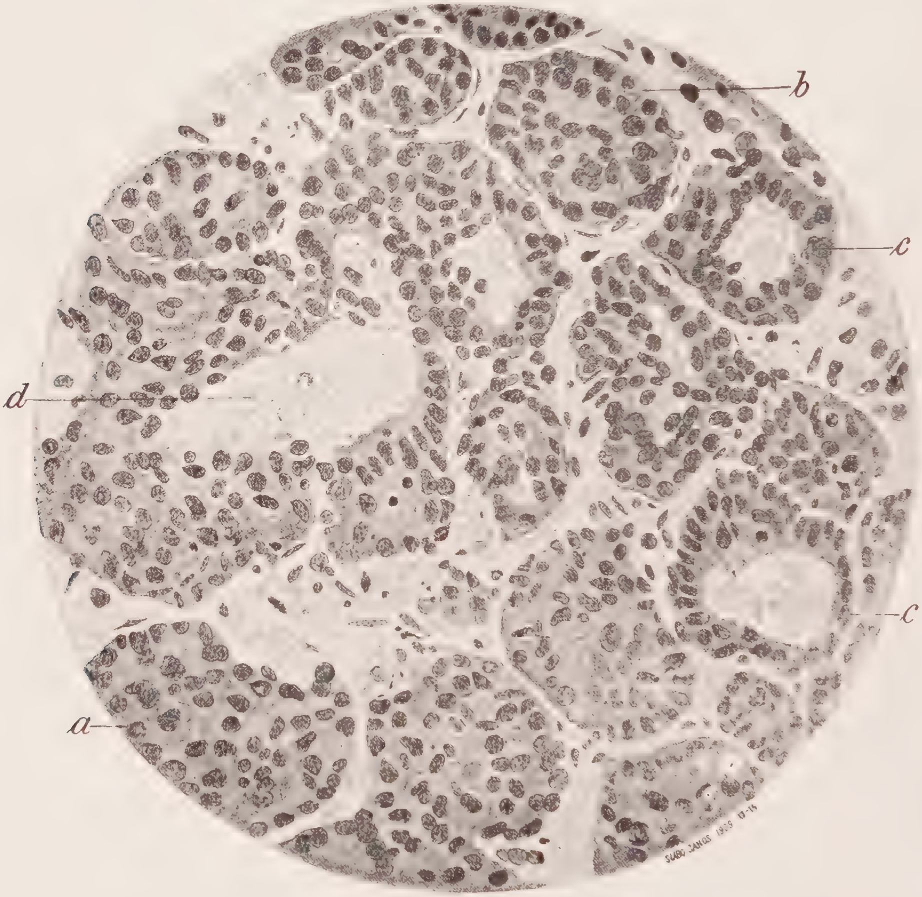


FIG. 467.—Liver cell carcinoma of woman 75 years old. a, compact nest; b, nest with bile-containing cleft formation; c, nests with lumen, containing bile droplets and debris, large lumen filled with detritus (V. A., 203, 1911).

where tumor cell columns touch the adjacent liver tissue, transition forms are frequently seen as illustrated by Goldzieher and Bokay. This form is called by some "malignant adenoma" (Frohmann, Ribbert and others, Siegenbeek van Heukelom, and Wegelin), by others "adenocarcinoma," because the tumor resembles liver tissue and demonstrates its malignancy by growth into vessels and other metastases. The author does not consider this name happily chosen and would call it "alveolar type" of carcinoma with columns or tubes, reserving the term "adenocarcinoma" for the second form (see below).

The types (*a*) and (*b*) may be combined, or there may be transitions from one to the other. It can be assumed that they originate in the liver cells particularly in cirrhoses, from the pseudoacinar parenchyma granules distinguished by hyperplasia. Muir and Goldzieher share this opinion.

Occasionally, the roughened angular branching figures of the overfilled bile capillaries (fig. 479) can be seen between the carcinoma cells as illustrated in fig. 466. This is of interest since it shows that the tumor, evidently malignant and showing a tendency to disintegration, can nevertheless produce bile. Perls first reported bile and bile capillaries both in the primary tumor and the metastases, conditions described also by Bock, Heller, Schmorl; Cloin and M. B. Schmidt even found bile capillaries in the metastases in the bones. Necker and Wegelin consider bile production by the tumor cells as the most important proof of their origin from liver cells.

Sokoloff's case is unique being a carcinoma with ciliated cells.

II. Cholangocellular carcinomas of the liver are less often found. They are usually adenocarcinomas (*a*) in the accepted sense. They start, although not without exceptions, in cirrhotic livers, the connective tissue of which is thickly crowded with branching plugs which frequently show gland-like lumena. There is a certain similarity to the bile channel proliferations in cirrhosis, and transitions are likewise seen from these to adenocarcinomatous proliferations with their atypical cell forms. The dainty gland imitations are composed of polymorphous high or low, sometimes stratified cylindrical cells. They are separated by connective tissue and some may contain granular bile in the lumen and cells. (*b*) They sometimes show transitions to large clumps of cells with marked polymorphous variations, including giant cells, especially if they invade the vessels, (branches of the portal vein), or tend to destroy the pseudoacinar granules (carcinoma solidum). The author saw carcinoma in a cirrhotic liver in a 44 year old man who died from hemorrhage from esophageal varices; likewise in a 62 year old drinker with severe ascites and metastases to the lungs. The origin of carcinoma cells from proliferating bile channel epithelium seems perfectly comprehensible. An adenomatous pre-stage is conceivable at times (see Saltykow).

Goldzieher considers bile channel epithelium the origin of the tumors resembling Krompecher's basal cell carcinoma (see under skin), which are made up of remarkably small polymorphous cells with nuclei rich in chromatin as well as of carcinoma simplex cubocellulare which have not the slightest resemblance nor relationship to liver cells (carcinoma solidum). The alveolar boundary is connective tissue. Carcinomas of the liver usually appear in advanced age (see Eggel), but also may arise in children, such as the author saw in a 15 year old boy. The newborn are not excluded (Ribbert, Wegelin, lit.) and even then there is an accompanying cirrhosis (see Herzog, Mieremet, exhaustive lit.). Hedinger saw carcinoma of the liver in two sisters.

Primary carcinomas of the liver rarely metastasize, and then mostly in the lungs, as recognized by Benda, in spite of the frequent invasion of blood vessels within the liver where they extend in strands over wide areas, in a peripheral or a central direction. Tumor masses which invade a large branch of the portal vein may be scattered in its branches without continuity. Although there is no doubt that this known distribution of some liver carcinomas simulates the picture of multiple tumors, on the other hand, it is not difficult to distinguish true multiple carcinomas, which actually occur (Adelheim), as well as primary multiple hyperplasias and adenomas. The portal lymph nodes are frequently infiltrated. Skeletal metastases are rare, (lit. by Blumberg). In a 33 year old man with a massive tumor of alveolar type in the right lobe of the liver, no cirrhosis, tumor partly hard, with smaller soft nodules (weight of liver 2590 gms.), the author saw enormous metastases in the pelvic bones, ribs, vertebrae, lungs and abdominal lymph nodes. A section from the pelvic tumor, which was larger than a child's head showed large fatty polygonal cells, resembling liver cells (see also cases of Prym and Karajannopoulos). In a 54 year old man with cirrhosis, the left lobe of the liver was diffusely infiltrated and enormously enlarged, weight of liver 2560 gms. Metastasis occurred in the abdominal lymph nodes, manubrium of the sternum, third to fifth thoracic vertebrae. Laminectomy for compression of the spinal cord with an exploratory incision, demonstrated the carcinoma. Carcinomas of the liver have also occluded the portal vein with consequent swelling of the spleen, gastric catarrh and ascites. Icterus may appear, at least more often in the liver itself. Grawitz reports death from hemorrhage into the abdominal cavity from a bulging globular nodule in a 52 year old woman.

It is better not to classify a carcinoma which springs from one of the large intrahepatic bile ducts, and is followed by severe icterus, among the primary hepatic carcinomas, but rather simply as a bile duct carcinoma. These will be discussed under tumors of the large bile ducts. Further literature in reference to carcinoma of the liver in appendix.

Small hypernephromas or nodules of adrenal tissue are not rare in the liver (Beer, lit.). Larger nodules to the size of hazel nuts or walnuts are exceptional (Schmorl, the author, Oberndorfer, Bindo de Vecchi, lit., Hirschler), among them malignant hypernephromas, (Pepere and also possibly the case of Donati, White and Mair). They may be mistaken for adenomas and carcinomas of liver cells.

Secondary Carcinomas.—They are continuous as retrograde invasions from the vicinity by way of the lymphatics, or they are true metastatic tumors. The latter are probably the more frequent and distribution and transport within the liver occurs via blood channels, a fact which can often be demonstrated. Some metastatic nodules therefore acquire a radiating arrangement.

The primary tumor, which sometimes is quite small, is often found in an organ which drains into the portal vein, *i.e.*, stomach, intestines, pancreas, pelvic organs, etc., and for this reason the cylindrical cell variety is the most frequent type. But every other type may metastasize and resemble the primary tumor, or be de-differentiated so to speak. Occasionally a retrograde route seems the only possible way in which a metastasis from a distant organ such as mammae has occurred, *i.e.*, through the hepatic veins (see Ziegler). The liver may be the only organ containing metastases.

From the material at the institute of Basle, the author has formulated the following figures relative to participation by the liver: metastases from carcinoma of the pancreas, 50.5%, carcinoma of the gall bladder 39.5%, carcinoma of the stomach 33%, carcinoma of the breast 32%, esophageal carcinoma, 23.5%, carcinoma of the thyroid, 18%, carcinoma of the uterus 12%, and in all carcinomas (1078 cases), 26.5% (I. Diss. Jasnogrodsky). In 1287 cases of carcinoma, Briese found the liver involved in 29.05%. Metastases to the liver are so common that they may be expected in every case, even in peripheral carcinomas. The author saw metastases in the inguinal glands and the liver from a very small carcinoma in the skin of the large toe. Metastases are so abundant and of such great size that the liver reaches the highest degrees of enlargement and weight. Christian reports a carcinomatous liver over 15 kgs. in weight which he found in a 62 year old man with carcinoma of the rectum. The rapid growth of metastases was well illustrated to the author in a case of a 60 year old man, who had been operated for carcinomatous ulcer, at which time no metastases were demonstrated. Five months later, a 5500 gm. liver was found riddled with large, soft, necrotic and hemorrhagic nodules. Death occurred from hemorrhage into the abdominal cavity from a ruptured tumor nodule as large as a fist.

Metastases are often seen as diffuse infiltrations of large areas of the liver without any marked change in the outer aspect. More frequently, large masses, or countless hard or soft nodules are found. The former, *i.e.*, the scirrhous forms, usually infiltrate the vicinity, while the latter, chiefly adenocarcinomas, displace adjacent tissue, so that the liver cell columns are pushed together concentrically and become dislodged, flattened, compressed and atrophic. Sometimes the nodules can be easily shelled out. If they are on the surface, the serosa covering them is more or less vascularized.

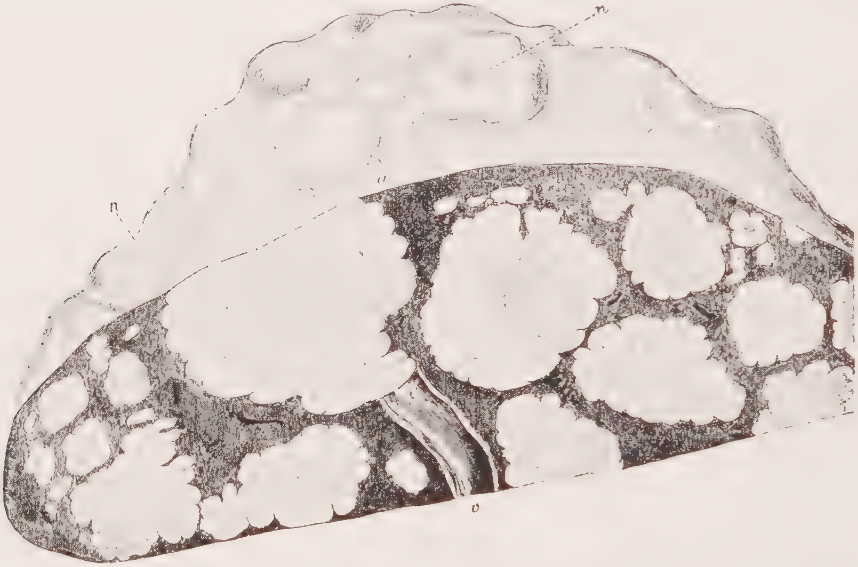


Fig. 468.—Secondary carcinoma nodules in liver from cylindrical cell carcinoma of stomach; n, so-called carcinoma umbilicus; v, hepatic vein with carcinomatous parietal thrombus; a, hemorrhagic infiltrated area; ⅗ nat. size.

The tumors are usually pure white in the beginning, but become altered by regressive changes such as fatty degeneration, necrosis, sometimes in the form of soft, or firm, moist or dry caseation and colloid metamorphosis, or by hemorrhages thus becoming yellow, yellowish brown or red and sometimes cystic. In the subserous solid tumors, central disintegration with scarring and shrinking, causes a sunken area, the so-called carcinoma umbilication which rises above the surface (fig. 468). This appearance it must be remembered, also occurs, although rarely in secondary sarcomas. Diffuse carcinomatous infiltrations are sometimes homogeneous and grayish white and may be dispersed as conglomerations of nodules, or as single nodules; at times they present very colorful pictures caused by necrosis and hemorrhage in both the tumor and liver tissue. Rare cases such as the following are also encountered: in a 44 year old woman with a small mammary carcinoma and involvement of axillary and subclavian nodes, the author saw a liver, externally smooth, with no typical carcinoma tissue on section but with necrosis of liver tissue and hemorrhages dominating the picture. Microscopically, occlusion of innumerable sublobular veins by carcinoma and infiltration into liver tissue could be instantly recognized. Where the tumor becomes established, either as nodules or infiltrations, the liver cells die, while the connective tissue is stimulated to various degrees of proliferation (see Ruhlemann). In rare cases we see scirrhous infiltrations with great abundance of scar tissue, so that only islands of soft tumor are seen within, and sometimes we cannot recognize even microscopically that liver tissue was ever present. Some carcinomas contain wide blood vessels in such quantities that they can be called "telangiectatic." In rare cases exsanguination into the abdominal cavity has occurred, (see observations above). Metastatic nodules may become mushy through softening, and present a pulpy, grayish red mass or a creamy yellow fluid in actual cysts. The latter process is especially frequent in colloid carcinomas, but also occurs in other forms so that the author in two cases suspected at first echinococcus cyst. In a 40 year old woman with a small fungoid, richly vascular cylindrical cell carcinoma of the pylorus, the liver, almost five kgs. in weight, contained many gelatinous, hemorrhagic, softened, vascular nodules. The largest, ovoid in shape, in the right lobe was 19 cm. in diameter, bulged hemispherically and fluctuated. It had been punctured to examine for echinococcus. Several subserous nodules, anteriorly to the right, and posteriorly to the left, were fissured on their surface, flooded with blood and ruptured, so that the soft tumor masses were prolapsed. The abdomen contained 2700 cc. of blood (see Bressler, lit. and comp. Salinger). In another case from a small, soft, bowl-shaped carcinoma below the cardia, a cystic metastasis the size of a child's head had developed in the liver, also suggesting echinococcus and calling for laparotomy. The erroneous diagnosis of echinococcus is occasionally made also in the presence of soft pseudo-fluctuating nodes. The author repeatedly saw cystic metastases from keratosing pavement epithelium carcinoma of the esophagus.

In two of these cases (men 43 and 44 years old) the liver was filled by partly solid, white, grumous, keratosing carcinoma nodules and partly cystic masses, which contained thick, stringy, clear yellow or yellowish brown contents, with a white carcinomatous wall. The nodules and cysts for the most part were not larger than a cherry. But on the whole, mucoid metamorphosis of metastases from a horny carcinoma is rare. In a third case (see fig. 469), a 55 year old man, the liver contained several cystic cavities, each larger than a fist, within the carcinoma which was composed of small angular and rounded cells showing a tendency to necrosis. In an 83 year old woman, the author saw many cysts, some of the size of chestnuts with watery contents, arising from carcinoma of the vulva; the tumors of the inguinal glands were partly cystic. Sometimes calcareous infiltration of metastatic carcinomas is found and the nodules are as hard as mortar. This was seen by the author in a 68 year old woman, in whom numerous calcified metastases up to the size of a child's head arose from a small cylindrical cell carcinoma of the pylorus causing the liver to weigh 3660 gms. The woman also had marked osteoporosis.

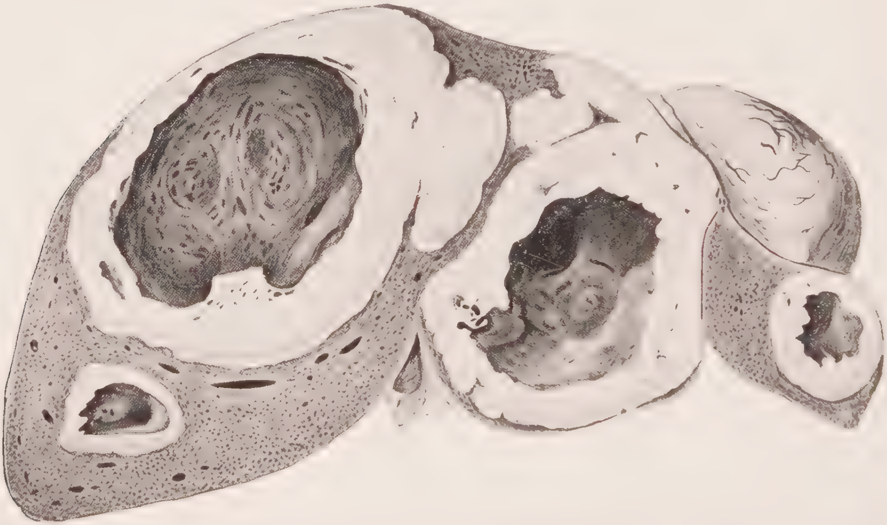


FIG. 469.—Secondary carcinoma with cystic softening in the liver from primary of esophagus of man 55 years old; ½ nat. size. (See text below.)

By continuity, the tumors appear from a gastric or gall bladder carcinoma (fig. 481).

Sometimes an infiltration from a carcinoma of the stomach or pancreas spreads by the retrograde route through the lymphatics and invades the vicinity and wall of the portal vein and bile ducts, so that white plexi diminishing in size and strands of hard nodules are drawn into the liver. This is also seen in carcinoma of the common, or of the hepatic ducts. If brown atrophy is also present, the much invaded organ need not be enlarged at all. Vogel, later Jacob and then Geraudel, reported on the modus of metastasis. Geraudel considers small and hard—and the author would add, angular and poorly defined—nodules, as lymphogenous in origin, while umbilicated, large, numerous, soft and rounded tumors are hematogenous.

The gigantic livers are most probably due to hematogenous metastasis.

Rupture of tumor masses and carcinomatous thrombosis in the liver veins occurs frequently, and other metastases, especially to the lungs, are favored; rupture into the branches of the portal vein causes hemorrhagic infiltrations (fig. 468) or infarct-like formations, (fig. 468) and necrosis (p. 899).

Occasionally, metastases in the liver arise from malignant chorionepitheliomas of the female genital apparatus (see there). Cases have occurred in which the uterus, vagina, etc., showed no tumor, while the liver was packed with white, and frequently bloody growths, in structure like malignant chorionepitheliomas. Such cases are called "primary," (B. Fischer, Paltauf). An ectopic chorionepithelioma of the liver may also occur with hydatidiform mole (Gurewitsch).

A mechanical, partial or complete obstruction of bile channels in the liver is due to the development of the metastases, which cause stasis, and bile absorption, expressed in a general icterus (lit. by Lepehne).

Hypertrophy and Regeneration of Liver Tissue

True hypertrophy of an otherwise healthy liver is rare, and must always be diagnosed with caution, since the dimensions of the liver vary within wide limits. Generally speaking, an enlarged liver is pathological (connective tissue induration, see Rossle). According to Beneke, remarkably large livers are seen in rachitic children. Partial (compensatory) hypertrophy is, however, not rare. It is seen in bulk when, *e.g.*, an echinococcus cyst occupies the right lobe and causes parenchymatous atrophy; the left lobe then may become extraordinarily large (Hollefeld, Ponfick and others). It is also seen in alveolar form of echinococcus. Compensatory hypertrophy takes place even in advanced age. A whole lobe may shrink to a small fibrous structure on account of previous inflammatory processes while the other lobe enlarges; substantial hypertrophy and hyperplasia can be observed in constricted livers, in the lobulated liver of luetics (lit. by Schorr), in the presence of numerous tumor nodules or cysts (cystic liver), in the rare large solitary cysts (Plenk), and also following large abscesses (see p. 914, an observation of the author). The individual lobules are plainly larger than normal. In reference to the extensive regeneration in the form of nodular hyperplasia (fig. 470) as occasionally observed after acute atrophy, see p. 910, and as to a similar change in Wilson's disease, see p. 970. A regenerative process is often active during an existing disease, but often only microscopically demonstrable as in the various forms of cirrhosis with their proliferations of liver cells and bile channel epithelium. Opinions are still divided as to whether liver cells may develop from bile channel proliferations; Ribbert, in opposition to Meder, denies it emphatically (see Hayami also, p. 926). After liver cells have been destroyed in a parenchymatous inflammatory process such as infections,—typhoid fever, small pox, etc., (see Huebschmann), chronic malaria (see Marchiafava and Bignami) and intoxications (experimental, and others with phosphorus and arsenic, see Heitzmann, lit.), there is always a well defined regeneration of liver cells and of bile channel epithelium (as in sublimate poisoning, see pp. 912–913). The young liver cells present the picture of "clear cells" as mentioned on p. 924. See Oppel, Manwaring (lit.) as to regeneration in experimental poisoning with phosphorus.

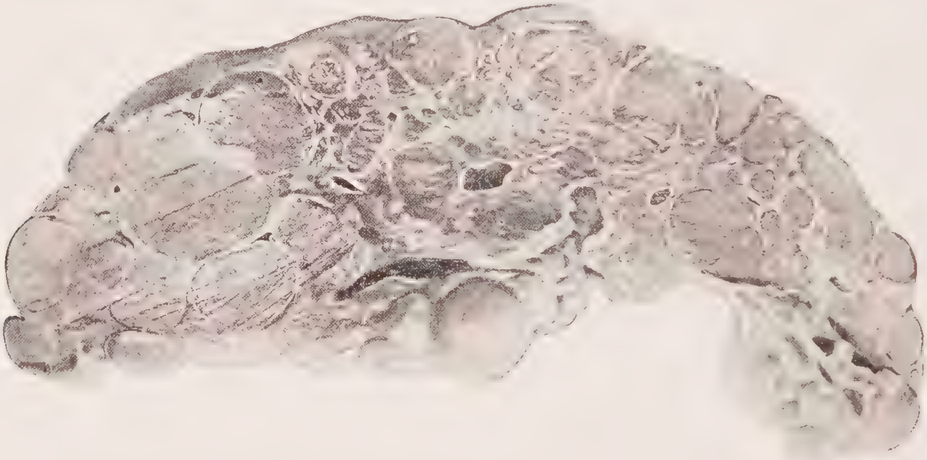


FIG. 470.—Nodular hyperplasia of liver in progressive lenticular nuclear degeneration (Wilson's disease) in girl 24 years old. Main section through organ; sl. over ½ nat. size.

It has been proved experimentally after injury to the liver (v. Podwyssozki), that regenerative proliferation begins not only in the immediate vicinity of the injury but even at distances. Both the liver cells and the bile channel epithelium participate, although Carraro believes only the liver cells take part. Ponfick has shown in animals, after partial removal of the liver, that the regenerative power is very great, in rabbits, after removal of ½ to ¾, according to Meister and Flock even ⅞, of the organ, the remaining lobules hypertrophy and become hyperplastic in a relatively short time so that the liver regains its original size.

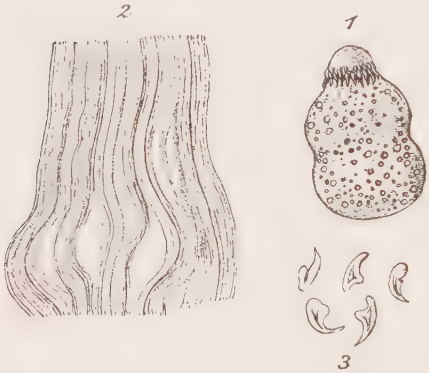
In trauma, especially rupture, if not fatal from hemorrhage, (lit, by Edler), an extensive compensatory proliferation soon takes place (Hess, Muir, Hallbauer); in fact Heile saw giant liver cells with 3 to 10 nuclei after traumatic, anemic, infarction (p. 899).

In Wilson's disease, or progressive degeneration of the lenticular nucleus, as well as in Westphal-Strumpell's pseudosclerosis which are, according to Oppenheim, but different types of the same disease (see under brain), a peculiar change occurs both in the brain and in the liver;

the latter is small and shows a coarse granular cirrhosis, with a coarse granular hyperplasia as in acute atrophy (see p. 910, and fig. 470, Yokoyama and W. Fischer). Refusing to accept the opinion of Meyer and Rumpel that this change in the liver has specific characteristics which point to a dysplasia or a developmental disturbance, most investigators come to the conclusion that there are various degrees of degeneration or necrosis and regeneration just as in the various kinds of cirrhosis especially the juvenile, mostly coarse grained forms (see Bostroem, Schmincke, Sjovall and Soderbergh). In some cases, necrosis is especially pronounced, (as in fig. 470); in others, there are various degrees of inflammatory processes quite marked in cases of Kleiber, Kubitz and Staemmler, v. Economo and others. Other authors do not recognize any appreciable difference in the microscopic arrangement of the liver cell columns and the vessels between this complex and cirrhosis (Meyer, Rumpel, Geismar). The etiology is obscure, and as Wilson has pointed out, there is a familial predisposition. In a few cases, syphilis was found (Homen), and in others suspected, but in many more no proofs were forthcoming (Wilson, Heinrichsdorff and others). Autotoxemia (intestinal?) is also considered as a factor which injures the liver and the brain electively in the lenticular nucleus; (compare elective involvement of the nuclei in icterus), or by some it is supposed that the liver might produce secondary injury to the brain (Wilson). The spleen is enlarged, occasionally ascites occurs. (See under brain for more lit.)

Parasites of the Liver

The echinococcus is the most important. There are three forms. (*a*) Echinococcus hydatidosus—cysticus—unilocularis—endogenes—E. hominis is the most frequent form (see fig. 432, p. 897). The echinococcus is the vesicular embryonic form, *i.e.*, the larval form of taenia echinococcus (or nana) of the dog infected by feeding on the infested meat of various domestic animals. The taenia are usually present in numbers, and consist of three segments, 4–6 mm. long,—not found in man. Its ova (oncospheres) which are passed with the canine feces, infect humans and occasionally also domesticated animals including birds. The ova after reaching the intestinal tract pass by way of the portal vein into the liver, but may also enter the chylous vessels and the lymphatic circulation; thus through the thoracic duct to the blood and the lungs, spleen, omentum, brain, spinal canal, bones, kidneys and subcutaneous tissue. Here the cyst (see under parasites p. 847) develops from the ovum (oncosphere), and reaches the size of a walnut in 2 to 3 months and is still an acephaliocyst (echinococcus cysticus sterilis). The cyst has an outer layer, the chitinous cuticle, which, in the beginning, is delicate and translucent, or coagulated, resembling egg albumen, or gelatinous, milky white and on section soon shows the characteristic lamellated parallel striations (fig. 471). After cutting the edges of the cyst, they curl inward (fig. 124). It contains clear fluid, (spec. gravity 1009–1015), rich in sodium chloride but practically devoid of albumen, it does not coagulate on boiling or after the addition of acid; succinic acid is present. If the cyst is in the liver, the liquid may contain sugar. The most important diagnostic proof is the demonstration of hooklets from dead parasites in the fluid obtained by puncture (fig. 471). The cuticle shows an inner thin granular parenchymatous layer. Small fish-roe-like, or granular thickenings of the germinal layer (fig. 473) visible as white dots by outside inspection of the cyst are its germinating capsules; their walls consist of the parenchymatous layer which lines the cyst, while it has also an inner cuticular layer. Occasionally, white, nodular, granular plaques, up to 0.5 cm. thickness are seen, these sometimes show a central depression in a smooth inner surface. The protuberances are described by Pommer as cuticular overgrowths. Approximately 5 to 15 echinococcus heads, scolices, are attached to the germinal capsule by a long pedicle. The scolices rarely exceed 0.3 mm. in length. They have a rostellum in front, four suckers, and a double circle of hooklets of two different sizes (fig. 471). In their interior, numerous granules are found. These scolices float in the water-clear fluid of the germinal sac and they are contractile, *i.e.*, able to retract and project the head. Scolices and germinal sacs may undergo cystic transformation, thus becoming daughter cysts, which in turn form new germinal capsules with scolices, which in their turn undergo cystic meta-



FIGS. 471 and 472.—Hydatid echinococcus; 1, scolex with head, double ring of hooklets, numerous lime granules within; 2, chitinous laminated cuticle with parallel striae; 3, loose hooklets (high power).

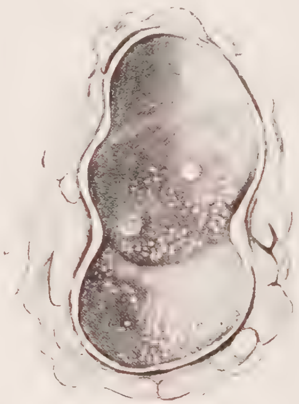


FIG. 473.—Cut echinococcus cyst in omentum; the white dots within are numerous breeding capsules; 2, larger bulgings of same; gardener 35 years old; $\frac{5}{6}$ nat. size.

morphosis becoming more daughter cysts. Some daughter cysts are sterile, *i.e.*, without scolices. The mother cyst may undergo complete atrophy due to the pressure of numerous daughter cysts so that the latter lie in a sac, or capsule formed by the surrounding connective tissue in which giant cells are sometimes seen. Daughter cysts may reach the number of several thousand. The whole echinococcus cyst may then weigh 10 to 15 kilos.

If no germinal capsules form and the cyst remains sterile, the acephalic cyst is of short duration. Those which die, soon calcify and may even be impregnated by bile. The cyst may remain the size of a fist to a child's head and on the inner surface form new germinal capsules and scolices, containing a clear liquid. This formation of new generations of scolices often gives the echinococcus long life, even 20 to 30 years (see Marchand).

(*b*) In contradistinction to this endogenous cyst formation, an exogenous cyst may also arise as in many domesticated animals especially pigs and occasionally in humans, (echinococcus granulosus—ocolicipariens—verterinorum). At the most these cysts reach the size of a hen's egg.

Daughter cysts may form independently of the parenchyma layer within the cyst wall, receiving an inner parenchyma layer and developing germinal capsules. During their growth they distend the wall of the mother cyst bulging it outward with bosses or diverticuli and finally rupturing outward, when they are represented as independent cysts. At the same time on the inner surface of the mother cyst new germinal capsules form.

(*c*) Echinococcus multilocularis (alveolaris, ulcerosus, alveolar echinococcus) is the third variety of this parasite. This form is frequent in some territories such as southwest Germany, northeastern Switzerland, Russia. It is very seldom observed in north Germany and in the islands, while the common echinococcus is quite frequent. At first the echinococcus multilocularis of the liver does not resemble a cysticercus at all but a change takes place in the liver combined with marked enlargement which sometimes resembles a scirrhous carcinoma, and has been mistaken for this until Virchow recognized its parasitic nature (multilocular ulcerative echinococcus tumor). In the differential diagnosis we must also take into consideration, mucoid carcinoma, cystic liver, areolar, honeycombed, locally massed, older abscesses, *e.g.*, from actinomyces.

The individual cysts are from microscopic size to that of a millet seed or a pea. They contain no fluid, but gelatinous lumpy masses with the characteristic parallel striations; they stain selectively dark red with Best's carmine stain (see Clerc, lit.); or the cysts contain scolices and hooklets. These cysts force themselves through the liver tissue, close against each other or hanging together, proceeding, according to Virchow, by way of the lymph vessels into which they enter. According to Friedreich, the parasite selects the bile channels first. But they may invade all systems and may reach the liver by way of the portal vein (see Clerc). They form folded and skeined chitinous membranes causing pressure disturbances; dissemination may take place even in blood vessels, although more frequently the vessels are occluded by endovasculitis. The liver parenchyma between the cysts undergoes atrophy or fatty degeneration and necrosis, both from pressure and from the toxic action of the parasites. The fibrous

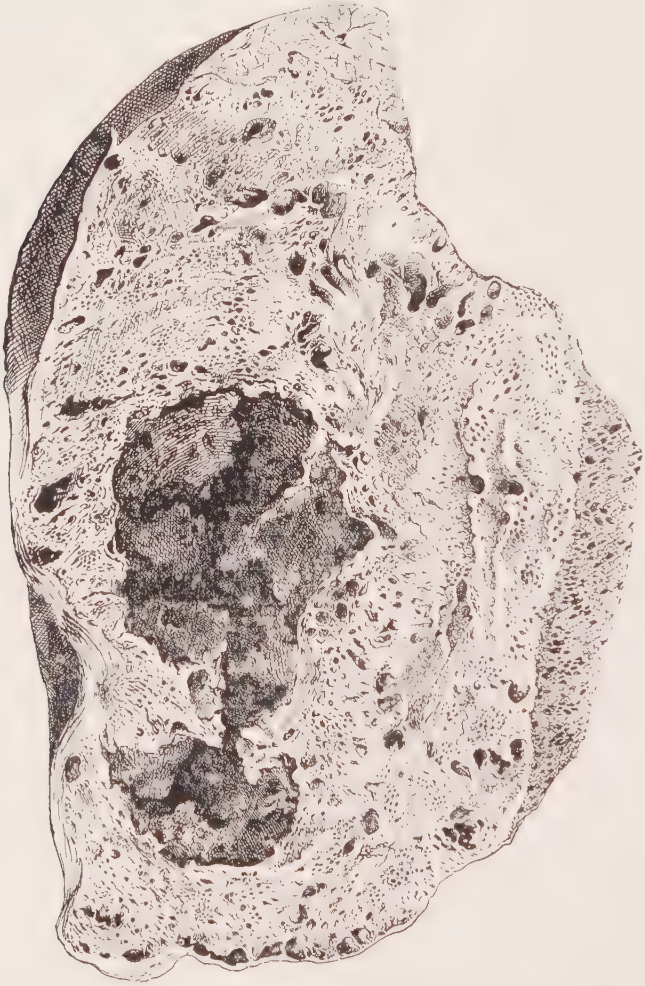


Fig. 474.—Multilocular echinococcus, alveolar echinococcus. Perpendicular section through r. lobe of man 30 years old. The liver olive green; in the large cavity pus of icteric color; membranes in bile ducts and branches of portal vein; in some places microscopic scolices with hooklets; 4/5 nat. size.

parts become thickened. The diseased portion may become stony hard showing neither fluctuation nor the hydatid bruit. Between the cloudy scarred masses as large perhaps as a fist, are "alveoli," round or branching clumps or smooth walled spaces—which, however, are not surrounded by a true capsule—filled with jelly-like fluid giving the whole focus a porous appearance. Microscopically, foreign body giant cells in the granulation tissue are seen lying against the membranes (fig. 475). Guillebeau and others, like Caesar, emphasize the similarity to infectious granulomas, *e.g.*, tuberculosis, particularly in the younger parts which are richer in epithelioid and giant cells. Caseation is also found (Mangold, Possett and others). Usually there is more marked bile channel proliferation. The gelatinous mass may be clouded by lime granules or fatty debris.

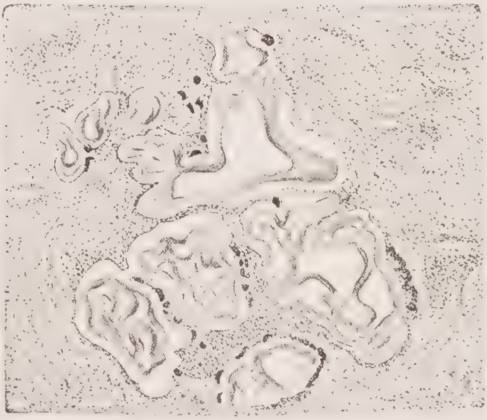


Fig. 475.—Multilocular echinococcus of liver. The finely striated animal membranes, usually collapsed in folds lie in cellular fibrous tissue; the black spots lying outside the cysts are giant cells, partly fused into syncytia (very low power).

The central connnective tissue septa often become necrotic from poor nutrition and saturated by bile, thus forming irregular, small or large (even beyond the size of a man's head), ulcerative cavities with roughened inner surfaces, the contents of which may be bile or blood stained and amount to many liters. If such a cavity is situated below the surface it may be palpated. If suppuration is added, the parasitic nature of the change in the liver can be recognized only with great difficulty. Alveolar echinococci of the size of cherries to hen's eggs are rare, and recognized macroscopically with the greatest of difficulty.

Perhaps a taenia other than the common form is the cause of these changes, but opinions are still divided on this point (Elenevsky). Vogler emphasized the greater delicacy and slenderness, length and slighter curvature, and the more striking length of the root processes of the hooklets of echinococcus multilocularis, and Posselt shares this opinion (see the feeding experiments by Mangold, and Zschentzsch, lit.). According to Melnikow-Raswedenkow, the presence of a granular parenchyma layer producing embryos of a different type on the outside of the chitin capsule as well as within is a characteristic of this echinococcus; this statement could not be verified by Mirolubow. On the other hand, Virchow, Hauser, Jenckel (lit.) state that the multilocular echinococcus is the same taenia as the hydatidosus. Posselt holds the opinion that frequency of the hydatid echinococcus is due to an abundance of sheep (not to dogs), while the multilocular echinococcus is due to cattle. He also points out that the latter was never observed in children, in whom the hydatidosus appears often enough.

The consequences of multilocular echinococcus are compression of the portal vein and bile channels with ascites and icterus. It may rupture into the pleural cavity, lung, gall bladder the inferior cava (Zschensch), etc., and then "metastases" occur. Splenic tumor is usually present.

True hematogenous "metastasis" in the lungs, brain (see there), bones (see there), is rare (see Biber, Clerc, lit.).

According to Elenevsky, primary invasion of the alveolar echinococcus may occur in other organs (spleen, adrenals). Hauser described an echinococcus multilocularis in the lungs and pleura.

Echinococcus hydatidosus most frequently elects the right lobe of the liver especially its upper part close to the diaphragm (see p. 915, under liver abscess for the anatomical explanation of this). It appears singly or multiple and develops slowly. It may reach the size of a man's head. (A specimen from a 74 year old man in the collection of Basle weighs 6 kgs.) When the duration is longer, proliferation of the surrounding connective tissue forms a secondary fibrous capsule around the cyst.

The statements made on p. 971 hold good in reference to the probable way by which the embryos of the hydatid echinococcus reach the liver (see Chiari lit.).

Course of the common hydatid echinococcus in the liver: the cyst may atrophy in its early stage frequently favored by bacterial, exudative and productive inflammatory processes in the organic membrane surrounding the parasites. The fluid content is partly absorbed, the cyst collapses and folds up. Old cysts frequently show a smeary caseous yellow mass on the inner surface and in the cavity understood to be the product of inflammation. It contains fat detritus and abundant cholesterin and cyst remnants. In greatly swollen gelatinous cysts, the fine striation of the membrane may become invisible in parts and often only the hooklets can be found. The caseous contents are, at times, saturated with bile, and microscopically bile clumps and crystals are seen. Again, they calcify and with them, the capsule. Often, in perhaps 50% of the cases, spontaneous cure is brought about, and such cases run a latent course. Living echinococci attract attention by circulatory congestion or by icterus from pressure on the hilum of the liver or directly on a bile duct, (lit. by Quenu). Others become dangerous by abscess formation and suppuration. After trauma or puncture, perhaps too by the advent of hematogenous pyogenic organisms (see J. Koch, Mehlhose), the neighborhood becomes purulent and the contents are destroyed by pus. This forms an abscess in which hooklets and rolled up remnants of the membrane are frequently found. The intact membrane of the hydatid cyst cannot be penetrated by bacteria. In a case of typhoid fever the blood serum of which agglutinated in a dilution of $1/200$, Trozier found neither typhoid agglutinins nor other antibodies in the fluid.

While spontaneous rupture is exceedingly frequent with hydatid echinococus, it is rare with alveolar echinococcus; see Posselt, lit.

Rupture into an adjacent cavity sometimes occurs from light trauma or without abscess formation when the adjacent parts undergo pressure atrophy. For instance, in a young man, the author saw rupture of an echinococcus cyst of the liver caused by violent dancing. If the sac ruptures into the abdominal cavity and the cyst contains pus, a purulent peritonitis results, quickly fatal; or if not purulent, there is a peritoneal irritation, more or less severe, which usually subsides (s. Ochlecker, lit.), but toxic symptoms are prominent, such as vomiting, diarrhea, urticaria, eosinophilia (not pathognomonic signs—Barling-Welsh). The consequences are more serious if the echinococcus cyst contained daughter cysts or they may be transplanted to the peritoneum and produce a productive inflammation with many giant cells (see p. 870). Development occurs in many places and the active general peritonitis resembles a tuberculous process (F. Weber and others). The result is usually fatal (see Kablukoff). The cysts may later be covered by adhesions and appear to be subperitoneal.

Sometimes embryos (scolices) may be liberated and transplanted after rupture of an echinococcus cyst, growing later into cysts and so-called foreign body tubercles, enclosing lamellae, hooklets or scolices (see Riemann). In other cases, rupture occurs through the diaphragm into the pleural cavity, lungs and bronchi (see p. 481), or into the stomach, intestines, pelvis (usually the right), rarely into the urinary bladder or vagina, as seen by the author in a 17 year old girl (see Schroeder, lit.). Rupture may occur into the bile ducts (the author) (lit. Carle), which, according to Quenu (lit.), causes cholangitis, and is the most frequent cause of icterus with cystic echinococcus. Rupture into the hepatic veins is rare, such as is shown in a preparation in the collection at Basle from a 37 year old man (included in the work of Deve lit.), nor is rupture into the inferior vena cava with pulmonary metastases or fatal pulmonary embolism frequent. Pressure of a large cyst may cause atrophy of a whole lobe of the liver, but the slow growth of the cyst permits compensatory hypertrophy of the parenchyma (see p. 969). Lit. by Peiper, E. IX publ. 1905; and in reference to surgically important localizations of echinococcus, see Frangenheim (up to 1906), A. Becker (up to 1908) and Parlavecchio.

Other Parasites of the Liver.—**Pentastomum denticulatum,** the larval form of pentastomum taenioides or linquatula rhinaria (a lancet shaped parasite living in the nose of the dog), is a frequent parasite of the liver. The larva inhabit the liver by preference under Glisson's capsule. Although in some regions it is common, (rare in Basel), it is of no particular importance. It appears infrequently in the spleen, kidney, lung, (subpleural), more often in the mesentery or intestinal wall (see Laengner). Since the parasite dies shortly after invading the body it is generally found as a small mass, calcified and surrounded by a dense fibrous capsule, no larger than a pea, sometimes crescent shaped or round and flattened. After dissolving in hydrochloric acid, the larva can be recognized at times; it is 2 to 4 mm. long with a spiny chitinous segmented cover over its cephalic end showing a mouth with four hooklets (feet). The adult parasite has been observed in man with the symptom of hemorrhage from the nose (Landon). Other parasites which can be mentioned are: cysticercus (rare), distoma as distoma hepaticum (fasciola hepatica, liver leech), distomum lanceolatum and distomum hepaticum (rare), distomum felineum (very rare), (see p. 856 in reference to these parasites). Distomum forms are essentially tropical, and cause grave changes in the liver such as large cystic sacs from dilatation of bile ducts in which the flat distoma are found. The changes resemble biliary cirrhosis (see Mebius, lit.). Ascaris lumbricoides is an infrequent cause of hepatic abscesses, p. 852. Psorospermia (coccidium oviforme), are rare in man, either within the liver, or its capsule, but they are frequent in rabbits, sometimes occurring in enormous numbers in the bile ducts, causing white caseous or purulent caseous foci (coccidia-nodules), which consist of dilated bile channels. The walls are lined by epithelium with more or less marked papillary proliferations so that the nodules resemble adenomatous tumors.

GALL BLADDER AND BILE DUCTS

Anatomy.—As Aschoff has stated, we may distinguish the following five layers in the gall bladder: mucous layer, muscular layer, fibrous layer, subserous layer and serosa. The last three may be grouped as a connective tissue layer. The scaffolding of the reticulated folds of the mucosa consists of fine fibres and small numbers of connective tissue cells (see Sudler). Luschka's ducts are eversions of surface epithelium and can be easily mistaken for the glands which are true mucous glands present only in the neck of the gall bladder. The former are branched with clubbed ends and may extend into the fibrous layer. The epithelial cells contain fat droplets, granules of precipitated absorbed biliary pigments and secreted mucus. (For the physiology of fat absorption, see Policard.) Small yellow villi and daintily arranged light yellow trabeculae, not infrequently seen against a grass green background are evidences of lipoid absorption by lymph vessels. The fat globules are present in the large cells by which the lymph vessels are completely filled. (Lymph vessels of the gall bladder—see Franke—see also anatomy by Testut, Shikinami.)

Malformations

The gall bladder is rarely absent, but the author has seen two cases in adults (lit. by Bubenhofer, Ewers). An anomaly which is not rare in the author's experience is that in which the fundus is kinked somewhat like a Phrygian cap, and this Bartel considers a sign of constitutional weakness of the organism with retarded development.

The opening of the papilla may be abnormally large, it may be located too high in the duodenum quite close to the pylorus, or there may be two openings. The common duct may be double (Meckel). The gall bladder has usually a free surface to the cystic duct with the exception of the area which lies flat against the quadrate lobe; but occasionally the liver completely surrounds the gall bladder with the exception of the fundus, or passes splint- or bridge-like over it. On the other hand, it may be entirely free, suspended only by the cystic duct (pedunculated, pendulum or floating gall bladder), and torsion of the pedicle, or volvulus may result. (In the case of Kubig the bluish black discolored gall bladder was twisted through an arc of 270°.) This condtion leads to hemorrhagic infarction and gangrene (Reichel, lit., Krabbel). The gall bladder and the transverse colon are, at times, adherent through a broad or narrow peritoneal band, the hepato-colic ligament, which is really an extension of the free edge of the hepatoduodenal ligament, into which the cystic duct dips. The gall bladder may adhere by a tape to the liver, and thus have a sort of mesentery. Konjetzny found the hepato-colic ligament in the newborn and in children in about 15 to 20% of cases, of which 60 to 70% were girls. It is of importance because (*a*) it favors calculus formation by biliary stasis (*b*) or causes duodenal or pyloric stenosis if it becomes taut through distension of the colon, with the gall bladder and liver firmly fixed (Konjetzny).

Congenital atresias of the bile ducts are interpreted and misinterpreted as primary malformations due to aplasia, or as results of intrauterine luetic or non-specific inflammations. Among these may be found (*a*) obliteration of the lower end of the common duct, allowing of no communication with the duodenum and (*b*) atresia at the beginning of the cystic duct. In the first instance, the common bile duct is absent, or not patulous, and, as one author supposed, had never become patulous, but this is an error, since the extra-hepatic ducts are patent in the very beginning, become solid for a time, until finally a lumen is reestablished (see Rietz). In such cases, the bile ducts may be untraceable from the hilum of the liver to the duodenum, and the liver presents the picture of biliary cirrhosis (see Harbitz, author's case, published by Feer; lit. in relation to newborn, case of Cesaris-Demel in an icteric child 3.5 months old). Occasionally, the common duct, in case *a* dilates and becomes cystic; the gall bladder may be absent, or rudimentary, or show cystic dilatation. The investigations of Beneke, by showing that obliteration occurs later, *i.e.*, there is a primary closure from within, have disposed of the conception of aplasia. Boehm and Busik explained the occlusion as a persistence of the temporary epithelial closure of the bile ducts, especially of the primarily hollow common duct; Simmel also speaks of a malformation; Thomson, Beneke and Flebbe (lit.), refute the supposition of its relation to lues, although the latter believes in inflammatory causes. But, according to the author, this view denies too much, since there undoubtedly occur congenital, *i.e.*, intrauterine gummatous cholangitides with stenoses following (see fig. 456; Sugi; Mathieu). Primary inflammation of the liver and its ducts as a causative factor (Frensdorf, lit.), is strenuously opposed by Elperin who believes in a mechanical cause, viz., passive distension of the bile channels through pressure of the lobulated liver, and subsequent atresia. Meyenburg considers that inflammation, specific or non-specific, must play a part in some cases, but in the majority, a malformation of the first anlage is the primary cause. The last word has not been said in this question (see also Konjetzny, lit.).

The so-called idiopathic choledochus cyst is an infrequently occurring, cyst-like distension of the extraduodenal part of the common duct forming a sac-like dilatation, and is due, according to Weiss, to an abnormal weakness of its wall, and according to Budde (lit.), to a primary diverticulum-formation from pancreatic rests. The wall may be stretched by closure of the papilla, and bile stasis, and a cystic tumor up to the size of a man's head may fill the abdominal cavity (cases Arnolds, Kremer—lit.,—clinically mistaken for echinococcus) (lit. Dreesmann, Wettwet, Weiss, Ebner, Heiliger, Mayesima, Bohm, Roberts, Seeliger, and especially Budde).

Inflammation of Bile Ducts and Gall Bladder, Cholangitis and Cholecystitis

Simple Catarrhal Inflammation of the Bile Ducts and Gall Bladder.—Inflammation may involve the gall bladder and bile ducts coincidently or separately; most frequently it is the duodenal part of the common duct which is involved, usually as an extension of gastroduodenal catarrh.

Sometimes simple catarrh is due to stasis of bile which, although normally sterile, is not bactericidal; in fact, bile is a fairly good culture medium for the colon bacillus, but this organism usually produces purulent inflammation. Phosphorus and arsenic also produce catarrh, especially of the smaller bile channels. Sometimes catarrh is ascending, or hematogenous, sometimes descending, as in severe infections such as typhoid fever, cholera, small pox, etc.; it is especially the hematogenous forms which first attack the interacinar biliary channels as cholangiolas, as Naunyn terms them. In typhoid fever the corresponding organisms are found quite frequently in the gall bladder and ducts (Chiari, Posselt. p. 795); the same is true of cholera (Eug. Fraenkel, Greig). See p. 991 for the ways by which bacteria enter the gall bladder. Investigations of retrogressive movements in tubular duct systems by Goldmann (lit.) show that ascent of particulate matter can take place in relation to the mucous membrane and independent of peristalsis and antiperistalsis. This is of great importance in ascending infections, for carbon, given by mouth, can be demonstrated in twenty-four hours in the bile from biliary fistulae. See Laubenheimer regarding the bacteriology of cholecystitis, also for cholecystitis and calculus formation.

Naunyn groups all the pathological processes in the bile ducts under the term cholangitis, but they cannot all be considered true inflammations.

Acute catarrhal swelling of the mucosa or thick, opaque, mucous secretion full of round cells can obstruct the common duct where it narrows towards the papilla or at the papilla itself. (Diameter of the 2.5 cm. long duodenal part is 2 mm.; the remaining part, 7 cm. long, has a diameter of 6 to 7 mm.) Since the accumulating bile is unable to force a passage in this direction, it of necessity enters the lymphatics and from these the blood. This is called catarrhal icterus, or duodenal icterus; according to Naunyn, it usually disappears in a few weeks. Since these acute catarrhal affections are usually quite mild and rapidly subside, they are only accidentally found at post mortem. Then the mucosa appears reddened, soft, swollen and covered with viscid grayish-white mucus, turbid from leucocytes. Suitable pressure on the gall bladder frequently forces from the papilla a tough, grayish-white mucous plug, but the weak secretory pressure cannot accomplish this. (See Robitschek and Turolt in relation to secretory pressure.) In many cases the mucosa loses its turgidity after death, and this type of obstruction cannot be demonstrated.

> **Translator's Remarks.**—So-called catarrhal icterus is discussed by Klemperer, Killian and Heyd, who, on the basis of the literature and an autopsied case, state that it is not a pathologic entity, but that three forms can be differentiated: (1) that due to obstruction of the common duct following gastrointestinal catarrh; (2) that due to degeneration and multiple necrosis of the liver (hematogenous), and (3) that due to cholangitis Arch. Path. & Lab. Med., 2: 631: 1926.

Chronic and recurrent catarrhs lead to permanent dilatation of the channels and thinning of their walls, and occasionally to a polypoid thickening of the mucosa. In older individuals, the trabeculae of the mucosa are more and more elevated into papillary growths. Obliteration from atrophy of an infiltrated wall of a large bile duct is very rare if no calculi are present. Inflammation of the smaller biliary radicles is especially apt to be recurrent, and may ultimately lead to fibrous pericholangitis and interstitial hepatitis of ascending, cicatricial, or fibrous character, in which bacteria ascending from the bowel play an active part, but such an interstitial hepatitis may develop, *e.g.*, from chronic poisoning by phosphorus.

> **Translator's Remarks.**—After cholecystectomy, the bile ducts dilate and there is frequently "incontinence" of bile. This may favor ascending infection.

Purulent and Necrotic (Diphtheritic) Inflammations of the Gall Bladder and Bile Channels.—They are usually a consequence of calculus formation, but are occasionally due to animal parasites. They may also occur in the course of severe infections such as typhoid fever, dysentery, cholera, pyemia, etc. The infection enters the ducts from the bowel or through the blood stream; stasis of bile favors its development. Metastatic abscesses are rare.

The author saw a case of pyemia subsequent to an osteomyelitic abscess in the soft tissues of the left thigh in a man twenty-two years old. On the smooth mucosa of the gall bladder, moderately filled with a greenish yellow thin fluid, were a fair number of small metastatic abscesses which protruded as pin-head size pustules, and on cutting produced a droplet of pus.

When suppuration takes place with occlusion of the cystic duct, not infrequently from calculus formation, empyema of the gall bladder results (pyocholecystitis). The organ may hold even one litre of turbid yellow or creamy pus, so that it has been mistaken for an ovarian cyst. In rare cases, a dissecting phlegmon of the wall is seen. When this is combined with a necrosing inflammation, the ulcerative disintegration of the mucosa may penetrate the deeper layers (phlegmon), and the tissues become soft, friable and bile stained. Large areas of the wall slough with the necrotic mucosa, and, what is most important, perforations appear within a short time. If into the abdominal cavity (lit. by Ullmann), the results are purulent or ictero-purulent general peritonitis, or encysted purulent pericholecystitis, or, in rare cases, a prehepatic, subphrenic bile abscess which may perforate later (see bile fistulae, p. 993). For abscesses of the abdominal walls and Luschka's ducts, see p. 997.

In typhus fever, the author saw homogeneous, grass green, sharp edged circumscribed necrotic areas in the fundus of the gall bladder; in these areas the wall was thinned, and at one place perforated like a sieve. The rest of the mucosa was smooth and red; no calculi; 100 cc. of dark green bile in the abdomen.

In hemorrhagic, phlegmonous, ulcerative cholecystitis with cholelithiasis, the gall bladder may reach a size exceeding that of a goose egg, have a dirty bluish-red color, with the serosa showing fibrinous adhesions to omentum or transverse colon. The stiffened wall, as thick as 0.5 cm., has mucous tags on the inner surface some gray, some dirty red; the content is an hemorrhagic, bile stained fluid. Purulent inflammation of the bile ducts is usually accompanied by, or an accompaniment of calculus cholecystitis, *i.e.*, the ducts may be the seat of primary calculus formation, or become involved in a purulent icteric pyelophlebitis, or in hepatic abscesses. The severe consequences of bile duct inflammation to the liver have been discussed under suppurative hepatitis, (p. 920). Pseudomembranous (fibrinous) inflammation of a superficial type also occurs in the bile ducts.

See Eug. Fraenkel and Much in reference to severe experimental hematogenous cholecystitis by para-typhoid bacillus B, (see p. 761). [See Mann, F. C., for the production of a violent specific acute cholecystitis by chemical means (intravenous injection of Dakin's sol.). Ann. Surg., 73: 24: 1921.—*Translator.*]

Chronic Productive, Fibrous (Fibroplastic) Inflammation.—This may follow chronic catarrh by the deposition of fibrous tissue in a network in the mucosa giving the appearance of calloused trabeculations; or the organ as a whole becomes fibrous and atrophic and shows a tendency to shrinkage. The same process occurs, but much less frequently in the ducts. In spite of this, the shrinking gall bladder may be much enlarged when stones are present.

The diffusely fibrosed wall simulates an artery, especially when the calloused outer wall is smooth and becomes calcified or even ossified.

Very frequently, fibrous inflammation is the primary stage of a granulating process following ulceration due to calculi, (p. 995). To the cholecystitis is added a chronic productive pericholecystitis leading to adhesions with neighboring organs, especially the colon and omentum. Adhesions occasionally strangulate the neck of the gall bladder, or the cystic or common ducts.

Gall Stone Disease, Cholelithiasis

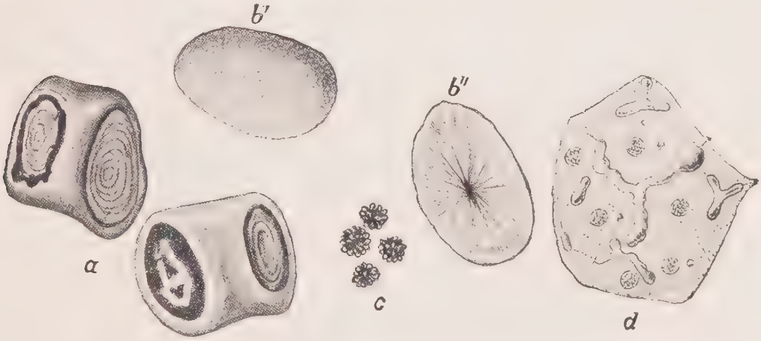
This is the most common and most important disease of the gall bladder and bile ducts. While many biliary calculi found at autopsy are known to have caused severe suffering, yet in many instances, stones found by accident never caused a symptom during life.

Gall stone formation is seldom seen before the twenty-fifth year. From then on its frequency progressively increases; women are much more subject than men. According to the autopsy findings at Basle, in 16,025 cases, males and females practically in equal numbers, gall stones were found in 10.9%; of those ⅔ were found in women (see Courvoisier). But, gall stones have been observed in children and even in the newborn, a condition also seen by the author (see Paulsen). Calculi vary in size and in number, ranging from minute sand-like granules, as high as 7000 or 8000 in number, to the large solitary stones which fill the gall bladder. The latter may weigh seventy to eighty grams; in fact, Ach reported a solitary stone weighing two hundred grams while moist, and one hundred and ten grams when dried (see also Lobmayer). Usually, however, the size is that of a pea or a cherry-pit. The smaller, the more numerous, but the size often varies widely in the same gall bladder and the most minute are found mixed with medium size stones. When the gall bladder is filled with many small loose stones, it feels like a bag of shot. In any given case the calculi are usually of the same composition, but occasionally a radiating cholesterin stone is found mingled with many of the composition of type B (see below).

Location.—Most calculi are found in the gall bladder, in gall bladder and ducts in about 9.3%, according to the autopsy material at Basle; they are rarely found in the ducts alone, as so-called "liver stones," but Vachell and Stevens once found five hundred and twenty liver calculi, thirteen hundred and seventy-eight grams in weight (see also Noguchi).

Gall stones in their chemical composition consist chiefly of cholesterin, bile pigments and calcium.

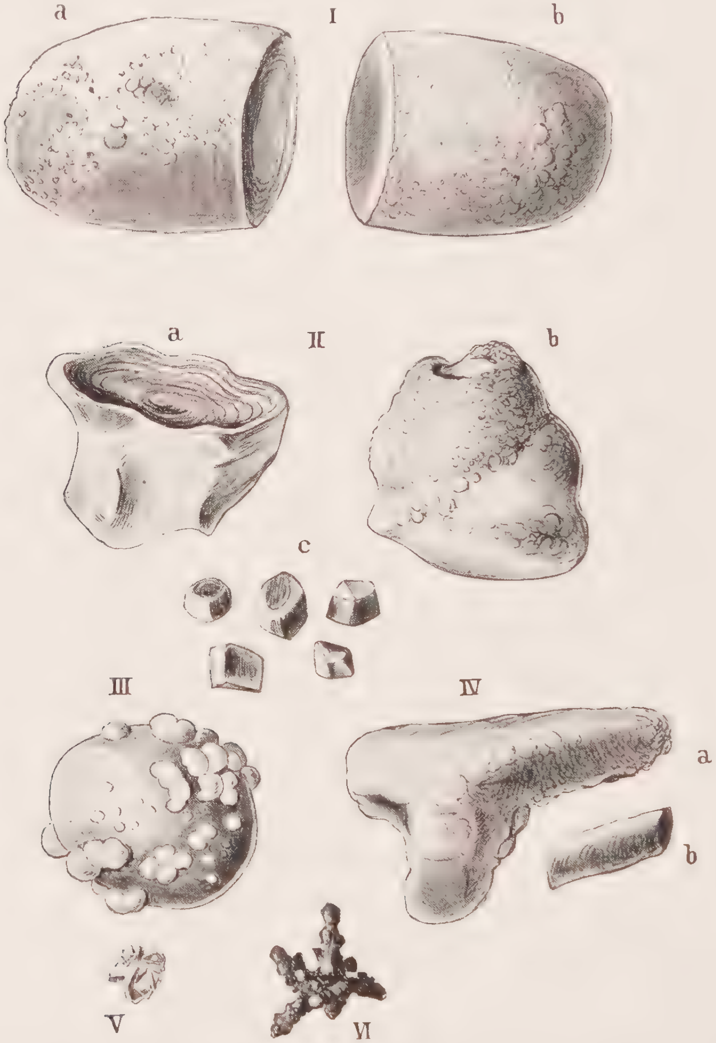
Cholesterin stones, if pure, consist only of cholesterin with a small amount of organic, and traces of inorganic substances. Kuru found a thin capsular layer of fibrin, and feels inclined to the assumption that this stone also has an inflammatory cause. They are usually rounded or oval, translucent, water clear or yellowish, smooth or granular. The author saw a concretion the size of a small pea in the neck of the gall bladder of a sixty-two year old man which consisted entirely of clear connected plates of cholesterin arranged at angles to each other (see fig. V). They are usually of the size of a cherry, have a fatty feel and are quite soft, easily cut and of light specific gravity. The fracture surface is radiating, ray-like and shiny (figs. b″ and b′). Since the crystals of cholesterin are arranged radially and protrude on the surface at different levels, the stone becomes finely granular. Frequently there is a soft nucleus, often very small, containing brown pigment. The color varies from yellow to brown according to the amount of biliary pigments. If calcium salts are present, we have cholesterin calcium calculi. These are opaque, chalky and laminated, with smooth surfaces.



FIGS. 476–479.—a, Facetted mixed gall stones (cholesterin-lime-bile pigment calculi); b′, pure cholesterin calculus, water clear; b″, composite calculus with pigmented fluid nucleus, a radiating shell of cholesterin and thin outer layer of cholesterin-lime (so-called combination calculus); c, bile pigment calcium calculi. a, b, c, in nat. size; d, dilated bile capillaries, after occlusion of the common duct by a gall stone; (high power).

Compound calculi, (Aschoff), have a radiating structure, usually with a pigment center. They have a cholesterin calcium capsule and are mostly solitary, but sometimes with type b. The author saw a case of hydro-cholecystitis with such a stone in the neck of the gall bladder, and in the water clear, slightly viscid fluid twelve rounded faceted calculi of identical composition. Occasionally, nodular cholesterin calcium deposits are found on the surface of such calculi (see fig. III, p. 986).

Cholesterin-bile pigment calculi (fig. a) are the most common; bile pigment, usually in combination with lime united with cholesterin, constitutes their main bulk (cholesterin lime). They vary greatly in quantity, size and shape, but very frequently are facetted. The chalky fracture surface shows concentric layers of lighter and darker strata. Sometimes one or more nuclei, a body and a cortex, may be differentiated (fig. b″). If the cortex is composed of cholesterin, the calculi are smooth, grayish-white, and of pearly luster; if it consists of pigment and lime they are dark, green-brown; if of calcium carbonate they are hard and white, smooth or nodular. Most cholesterin-bile pigment calculi are soft and easily crushed. The appearance of the fracture surface varies according to the proportion of the different constituents. Usually the nucleus is brown, soft, and greasy; according to Lichtwitz, it is coagulated colloid



Figs. 480–486.—Various gall stones. I. a, from the ileum; b, from the gall bladder. Stones from same case and fitted together. II. Large facetted gall stones from the gall bladder of a 23 year old woman. Calculus b, fits with its convex base into the concavity of a. From the same case, 5 small facetted calculi C. (there were numerous others). III. Combination calculus with rounded outgrowths of cholesterin-calcium. Cross section showed brown center (nucleus) covering of radiating cholesterin, cortex of cholesterin pigment calcium; woman 54 years old. The gall bladder contained yellow viscid bile. IV. Calculi from the common (a) and from the hepatic ducts (b). V. Rare cholesterin calculus from a man 62 years old from neck of gall bladder (see text, p. 985). VI. Coralline pigment calcium calculus from gall bladder of woman 60 years old. There was another similar; bile dark green; mucosa similar and without scars; all calculi, ⅞ nat. size.

material enclosing bilirubin lime. Crystallized cholesterin is seen within in plates, spicules or nodules. These calculi disintegrate easily in the air, but may be kept in 2% formalin solution. (See Ribbert's work on the formation and structure of gall stones.)

Pure bile pigment calculi are rare. They are yellow brown, green or black, small, friable, rounded or angular, light in weight.

Pigment lime calculi are dark, blackish green, usually small, rarely the size of a pea, often exceedingly numerous, very hard, nodular and of mulberry type; occasionally spicules radiate from one center.

Pure calcium calculi consisting of carbonate of lime are white or gray-white, nodular, hard, heavy and very rare.

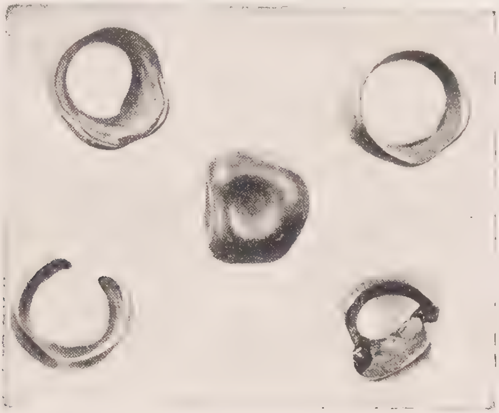


FIG. 487.—Gall stones spontaneously dissolving in woman 57 years old; no gall stone history; about nat. size.

The usual shape of the pure cholesterin calculus is globular or ellipsoid. The shape of common mixed calculi is concentrically round, but also poly- or tetrahedral, and their original form is modified by further growth in a limited space. In the bile ducts, the calculi are especially rich in bilirubin lime (see Hoffmann) and are sometimes cylindrical; in consequence of secondary deposits they show lateral prolongations. A solitary calculus of the gall bladder may fill it like an egg-shaped casting. If only a few large stones are present their corresponding surfaces touch and fit together as if molded with their concave and convex surfaces corresponding. As a few larger calculi increase in size simultaneously in limited space, they press against each other and thus develop facets; otherwise, lying together, they may mirror the form of the closely fitting gall bladder. The facets of the small, freely movable stones are due to unequal appositional growth on their different surfaces (see Aschoff), and their shape, as shown by section, is usually determined by the shape of their nucleus. No grinding down takes place. So-called carious calculi are those which are friable, probably because of the disintegrating forces of bacteria (rare), although Hansemann suggests the solvent action of bile as a factor; he succeeded in dissolving gall stones in dog bile. That a similar solvent process is possible in human bile is doubted by Aoyama. But Hedinger has recently reported an interesting human case showing that it may occur. After suitable treatment, it can be demonstrated microscopically by sectioning the calculi, that an organic rosette-like scaffolding of protein is present in common stones and much better developed in calcium rich stones than in those of pure cholesterin (see Aoyama lit.) (see Cole in ref. to x-ray diagnosis of gall stones).

For the formation of gall stones, bile stasis and probably also inflammation of the mucosa are essentially responsible; the latter may occur subsequent to stasis or independent of it. The most important chemicals are cholesterin and lime.

Naunyn's teaching which looks upon bile stasis as the underlying factor in calculus formation, and sees in the epithelium the immediate producer of the materials for stones, designates this process as a desquamating, calculus-forming angiocholitis which is induced by bacteria.

According to his investigations, there are two causes at work. (1) Calculi may form from disintegrating epithelium of the gall bladder or bile ducts (*a*) because from this epithelial debris, hyalinized myelin clumps consisting of cholesterin swell and conglomerate into larger masses thus forming a nucleus, (*b*) there appear soft lumpy masses of disintegrating epithelium covered by myelin, *i.e.*, true calculi which enlarge by further deposits. (2) In consequence of angiocholitis or cholangitis catarrhalis, protein-containing secretions of the mucosa produce a grumous, brown thickening of the bile by precipitating bilirubin-lime. This amorphous sediment consists of cholesterin, fat, bile-acid-alkali salts as well as bilirubin calcium and the protein-containing substances. Concretions then form in two ways: (*a*) the soft clumps are coated with a thin hard capsule of bilirubin calcium; the soft nucleus may be transformed by the crystallization of cholesterin while the bilirubin calcium sinks into it as nodular masses. Both adhere to the inner surface of the capsule while the fluid parts collect in the nuclear center; (*b*) from the amorphous sediment, the solids, crystalline cholesterin and amorphous bilirubin-calcium, are precipitated and thus form a soft capsule while the fluid substances gravitate to the center. These tiny calculi enlarge by the addition of new layers of cholesterin, pure or mixed with bilirubin calcium. According to the conception of H. Meckel von Hemsbach, developed by Kretz, cholesterin then infiltrates the calculus and crystallizes while the cholesterin already present recrystallizes in radiating directions, so that pure cholesterin calculi could arise secondarily from cholesterin-pigment-calcium calculi.

But the possibility of this process is not accepted by Aschoff and others; indeed Lichtwitz (lit.) considers the Aschoff-Bacmeister theory of only "primary" stones, as the rational view.

In recent times, other teachings have been urged. Most of them disagree with Naunyn's theory, but even among themselves there is considerable difference of opinion especially regarding the initial processes and the mechanism of cholesterin precipitation (see Tudichum, Gerard, S. P. Cramer, Boysen, Aschoff, Hirsch, Bacmeister, Lichtwitz, Kretz, Schade). It was demonstrated that cholesterin may precipitate in considerable quantity from filtered sterile bile kept at body temperature, a process, which according to Bacmeister, may be accelerated and intensified by the presence of protoplasmic substances, particularly desquamated gall bladder epithelium. Nevertheless, in animals, in spite of increased cholesterin content, it has been impossible to precipitate cholesterin in sterile bile (Naunyn, Kretz). Schade and later Lichtwitz (lit.), are more explicit in defining the colloid chemical conditions under which cholesterin precipitates. Cholates and soaps act as protective colloids in the solubility coefficient of cholesterin. Bile is a colloid protected supersaturated solution. Disturbances in the balance of these colloids causes precipitation of cholesterin, a sedimentation in the solution. According to Kretz, the essential point is the presence in the organism of a stable colloid-crystalloid solution which may coagulate upon the addition of secretions, blood, etc. The process may be compared to electro-plating. There are many controversies in reference to the source of the bile cholesterin, but whether it comes from the epithelium of the gall bladder wall, or from the liver as a product of general metabolism cannot be discussed here; see Nathan for lit. regarding the cholesterin content of bile. It has been demonstrated further that certain bacteria (b. coli and typhoid) bring about decomposition of bile, *i.e.*, bile acid salts, which are the solubility factors for cholesterin; these are broken down with consequent precipitation not only of cholesterin, but of all other component elements of biliary calculi such as calcium phosphate, calcium carbonate, magnesium phosphate, bile pigments, etc. (see Gerard, S. P. Cramer, Exner and Heyrowsky, Philipowicz, Emmerich and Wagner and others). While Kretz (Naunyn) believes in an inflammatory origin for all gall stones, Rovsing, in contradistinction, holds responsible a non-bacterial precipitation of bilirubin calcium due to excessive concentration of bile. It was also assumed that overdevelopment of mucous glands in which lime is formed, and the hypersecretion of mucus in infected gall bladders, *i.e.*, catarrh, increase the calcium content of bile, but Lichtwitz and Bock could not find a difference in the lime content of the bile from normal and inflamed gall bladders. Lichtwitz believes that every stone commences with a nucleus produced from bile sediment, and around this, either cholesterin is deposited radially, or colloid in concentric layers, and the latter takes place the more quickly, the richer the colloid content. It doubtless is greater in inflammatory conditions.

In view of such controversies, the question arises, is it proper to assume with certainty either a non-inflammatory or an inflammatory cause for calculus formation as is done by Aschoff? This is difficult to decide, because a very slight, momentary cholecystitis need not leave microscopic residue, and the finding of sterile bile does not prove that it has never been infected. But it does seem rational that a radiating cholesterin calculus occluding the neck of the gall bladder favors infection, and incidentally becomes a "combination stone," (see below), although the assertion of Aschoff and Bacmeister must first be proved, viz., that in the majority of cases the disposition to inflammatory calculous troubles is caused by radiating cholesterin stones, (see the case mentioned, p. 985 with 13 combination calculi). Further, according to Aschoff, the presence of a so-called combination stone is proof that a non-inflammatory period which supplied the nucleus for radially arranged cholesterin, must have preceded the inflammatory period which supplied the strata of laminated cholesterin-pigment-calcium substances.

As to the **etiology,** the first question is the influence of foods, especially those rich in fats and cholesterin as well as those containing lime. These questions are answered contradictorily. Thomas found that the cholesterin content of the bile was independent of the quantity in the food, and Jankau saw no increase in spite of heavy intake. On the other hand, Aoyama believes his experiments show the reverse, and sees in the differing foods, a factor which explains the frequency or rarity of cholelithiasis in different countries, for instance, its scarcity in Japan (see also Miyake). Some speak of a "constitutional" high cholesterin content of the blood, and thereby of the bile, while Chauffard and Grigaut demonstrated that the cholesterin content of bile is independent of that in the blood. Aschoff's assumption of a cholesterin diathesis amounting to a change in the total cholesterin metabolism, and particularly in its excretion in the bile, is disputed by Lichtwitz (lit.). The latter also believes that no guilt in calculous formation has been thrown upon pregnancy with its increased cholesterin metabolism (Klinkert, Chauffard). Recently, it has been put forth that lymphatism and other constitutional factors such as heredity are elements in the etiology of cholelithiasis (see Zellweger, Bartel, Hart lit. J. Bauer).

Of great importance, indeed, according to some the only actually proved cause of cholelithiasis (comp. Hofbauer), is **bile stasis** such as is seen frequently in tight lacing and the restriction of space in pregnancy.

Stasis permits cholesterin precipitation on the one hand, and favors ascending infection from the bowel on the other, with possible decomposition of the bile and inflammation of the walls of the gall bladder and ducts. Many bacteria grow well in bile, especially if stagnant (lit. by I. Koch). Although normally the bile contains no micro-organisms, (see Eug. Fraenkel), it is erroneous, as emphasized by Futterer, to consider bile antiseptic, as was formerly done. But Vetrano (lit.) observed bactericidal activity on pneumococci, antitoxic properties for streptococci, and Beitzke saw bactericidal effects on b. prodigiosus.

Bacteria may reach the gall bladder and bile ducts in several ways: (*a*) ascending from the bowel, (*b*) hematogenous, by the blood to the liver and excreted in the bile (see Biedl and Kraus, Chiari, Forster, lit. by Cannon), perhaps also (*c*), as is assumed by J. Koch, Quenu, Kwasniewski, they pass directly from the blood into the wall of the gall bladder and from thence into the bile. Their mere presence does not ipso facto cause disease. In typhoid fever, the bile always harbors bacilli but they do not necessarily establish gall bladder disease (see Hirsch also). But in the presence of calculi, it is extremely likely that slight abrasions of the mucosa occur into which pathogenic bacteria can invade, the quicker if they increase in number and virulence in stagnating bile. The chief offender in (*a*) is the bacillus coli communis. It is found alone chiefly in non-suppurative cholecystitis, either calculus or non-calculus, and calculus cholangitis, usually in the contents of these passage-ways; in suppurative conditions, staphylococci and streptococci are usually admixed (v. Mieczkowski, Hartmann). Gilbert in investigating seventy gall stone cases, found B. coli communis alive or dead within the calculi in one-third of the cases; typhoid bacilli were also found quite frequently. Bacmeister, on the other hand, believes that the bacteria invade the calculi secondarily. Miyake and Mignot and others, produced concretions, although not true multiple calculi, by the injection of pyogenic organisms; others made them in vitro with typhoid and colon bacilli and staphylococci. Therefore the importance of bacteria in calculus formation cannot be doubted, especially the part played by the typhoid bacillus, (Quenu and others), but the emphasis on the role of the latter is considered by some as a gross exaggeration (Bader, Eug. Fraenkel). In rabbits three weeks after immunization against typhoid bacilli, Emmerich and Wagner found cholecystitis with calculus formation after injections of typhoid bacilli into the gall bladder, (their probable relation is discussed on p. 990, also lit.). The increased disposition to calculus formation with increasing age may be explained perhaps by the greater difficulty in emptying a flabby gall bladder leading to stagnation of its contents and to more ready ascent of intestinal bacteria.

Calculi may also form by encrustation on blood coagula. In severe venous stasis, hemorrhages from the mucosa occasionally occur. Epithelium, devitalized, and shed in masses, can also become encrusted. Hansemann saw cholesterin-pigment-calcium concretions around silk thread in a duodenum seven months after operation for pyloric carcinoma (see also Kehr). Kratz considers Hansemann's case a demonstration of his theory (see p. 989), since the threads acted like drains and conducted a slight continuous inflow of coagulable secretion into the bowel contents, consisting chiefly of bile. Thus the conditions of colloid precipitation with crystalline deposits were fulfilled.

Consequences of Biliary Calculi.—This has been discussed in part under inflammations, and will be dealt with in greater detail in later chapters. A short summary follows:

Movements of Gall Stones along Normal Channels—Passage into, and Impaction of Calculi within the Bowel.—Calculi are sometimes removed by becoming fissured, cavernous, roughened, carious, disintegrated or fractured, when they may dissolve in the bile (Meckel von Hemsbach). Bacteria may assist or be the chief instrument. We distinguish therefore, a so-called carious and a smooth dissolution. Disintegration of calculi sometimes occurs in the bowel.

Most calculi do not move, but if their passage through bile ducts is obstructed, there is produced the exceedingly painful syndrome of gall stone colic with or without icterus, accompanied by vomiting and fever and lasting for hours or days. According to Aschoff, the colic is caused by a pull on the roots of the gall bladder consequent to a calculus lodged in its neck or in the cystic duct, or from the muscular contractions of an hypertrophic gall bladder. Spasms of the cystic duct cannot be an important cause since it is too poor in musculature, but it has many nerves and ganglia. Colic may occur without calculi from inflammation of the large ducts and especially of the gall bladder (see lit. by Boix); indeed, according to Riedel, 80 to 90% of cases of so-called gall stone colic are only painful expressions of inflammations of the gall bladder, usually with hydrops. But in the presence of a calculus, it is the pressure in the distended gall bladder as the stone is driven toward the cystic duct which induces the colic; the attack ceases when the stone has passed or when it has slipped back into the gall bladder (Riedel). According to Schmieden, colic can be caused by stasis alone from valve closure in the cystic duct.

Obstruction in the cystic duct may be caused by contortion. Even very small calculi, of 2 to 5 mm. in diameter are stopped occasionally, but the duct may also become sufficiently dilated to allow a calculus of the thickness of a thumb to pass through. The otherwise roomy common duct presents an obstruction to many calculi at the place where it suddenly narrows to enter the duodenal wall (see p. 982), but by back pressure, the normally low pressure of the bile may be so increased that the opening is sufficiently enlarged to permit the passage of calculi of the size of peas or somewhat larger (see in chapter IV, under "narrowing and closure of bile channels" and under icterus, for the consequences of obstruction of bile channels by calculi).

Passage of Gall Stones through Fistulae.—As we have seen, it is necessary for a calculus to be quite small in order that it pass through normal channels. Larger stones, by pressure, may ulcerate into surrounding hollow organs as a sort of passageway becomes enclosed by adhesions. If this occurs directly, it is called a direct fistula; in an indirect fistula, a bile abscess is situated between the bile channel and the hollow space into which the calculus escapes.

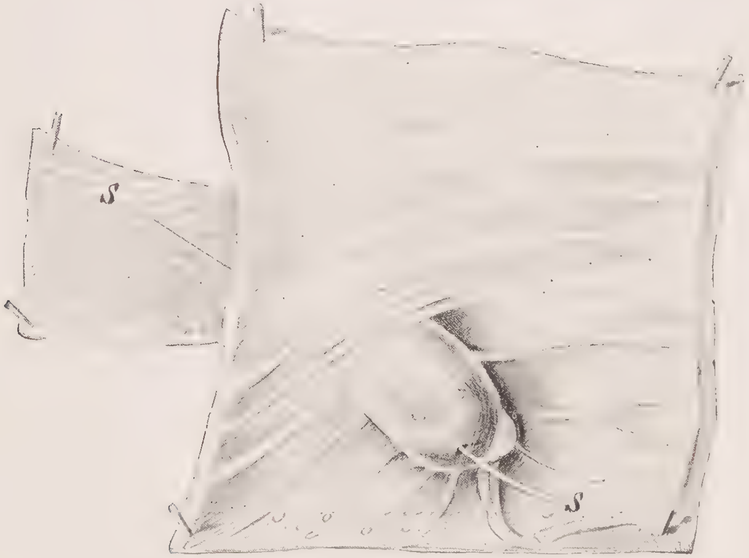


FIG. 488.—Calculus the size of a hazel nut in common duct. Fine choledochus-duodenal fistula; the probe S passing the stone leads into the markedly dilated common duct which, cut open, shows its inner surface net-like and granular S; to the right in the picture, behind the fistulous opening, the duodenal papilla through which the common duct is easily probed. In the markedly dilated gall bladder were three common calculi as large as peas; woman 64 years old with pulmonary phthisis; 7/8 nat. size.

Calculi impacted in the common duct reach the bowel through a choledochus-duodenal fistula. The communication is usually developed between the anterior wall of the upper section of the intestinal part of the common duct and the descending duodenum. The fistula of the gall bladder joins the fundus with the transverse colon, especially the right colic flexure, or more frequently, the posterior wall and neck of the gall bladder with the duodenum above the papilla. Fistulae into the stomach are rare; the same is true of those into the ileum, skin about the umbilicus or elsewhere, into the genito-urinary or respiratory organs, (see Ido and Yasuda), or into the portal vein. Occasionally there are several fistulae. Even the largest of stones may eventually reach the bowel through these communications, in fact, they may be large enough to remain in the ileum usually in its lower portion, especially when they are turned transversely. The intestine contracting down on them has caused ileus. The fistula may sometimes lead to a sort of spontaneous cure of the cholelithiasis. Fistulae rarely close completely; if they do, they have usually been in the duodenum. If the opening is too small to permit the passage of the calculus, a permanent fistula results.

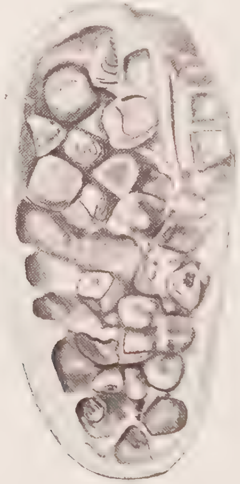


Fig. 489.—Gall bladder with so-called "walled in" stones. Cross section. Wall thickened; the cells contain stones, some have fallen out. The slight amount of gall bladder contents was cloudy thick muco-purulent containing free stones; woman 69 years old; 7/8 nat. size.

Local Changes in the Gall Bladder and Bile Ducts in Consequence of Calculi.—The discussion first must deal with the direct local effects of calculi and their after results. In reference to dilatation of the gall bladder, see p. 997.

That part of the gall bladder wall in contact with a calculus for any length of time frequently shows atrophy of the mucosa. Corresponding to the form of the calculus, actual facets may develop which are outlined by the fibrous tissue which replaces the mucosa like a linear wall.

The superficial losses of mucous membrane often heal to a smooth surface. Deeper ulcerations result mostly from pressure and the necrotic tissue may be thrown off by circumscribed suppuration. Not rarely, the entire mucosa is destroyed by the ulcerative process.

Sprengel denies the possibility of ulcers from pressure, but Grube and Graff defend their occurrence.

Deeper ulcerations may heal with subsequent contraction of radiating scars. The gall bladder as a whole may shrink and grow firmly around the stones.

The author saw an unusual case, (65 year old woman), in which the gall bladder appeared like a smooth cylinder the size of a thumb closely surrounding three large calculi touching each other closely. In the fundus were spaces the size of a cherry, with facetted walls covered by scar tissue, each of which contained a facetted stone.

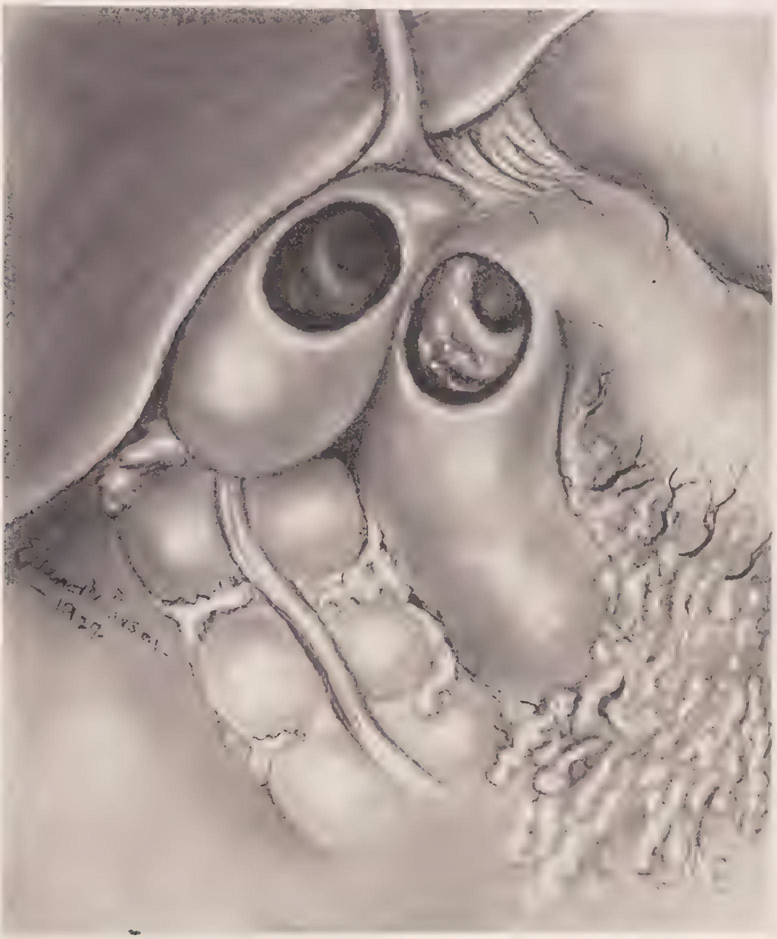


Fig. 490.—See Fig. 491.

Through scar formation there result also the so-called attached or impacted stones which appear never to have been in the gall bladder lumen at all.

In the case of these diverticuli or honey-comb cavities containing calculi it might be of importance to know whether the original site of the calculi was in a distended Luschka's duct.

Annular constrictions may give the gall bladder an hour glass or rosary appearance, when the cystic duct becomes obliterated. If the calculi are expelled and an ulcerated mucous surface left behind, the walls of the gall bladder grow together by granulation and the lumen entirely disappears, thus changing the gall bladder into a solid fibrous, often calcified, structure the size of a bean. If the ulcerations, usually circular, penetrate deeply, the serous surface of the gall bladder will show a productive pericholecystitis which favors adhesions to neighboring organs. If perforation occurs, it may lead to the formation of a direct or indirect fistula. In the latter fistula, a circumscribed abscess first forms. But if the

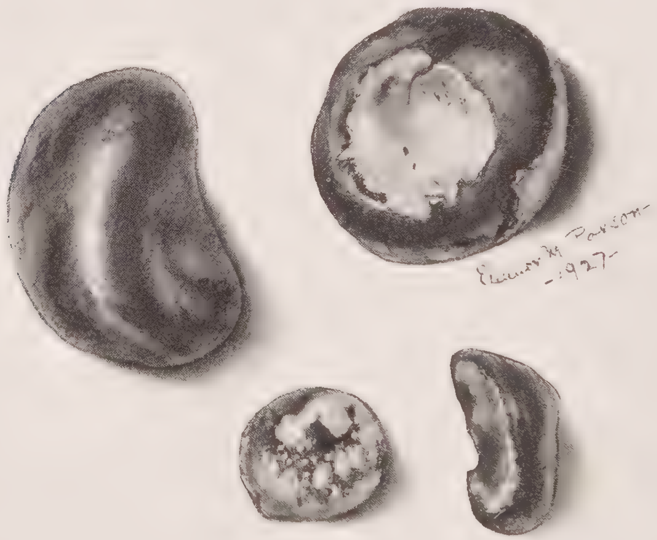


FIG. 491.

FIGS. 490–491.—Spontaneous cholecysto-duodenostomy caused by ulceration of gall stones through the gall bladder and duodenal walls. The gall stones, as in fig. 490, were so large that they could not pass through the opening but produced obstruction clinically identical with pyloric obstruction. Since the patient, a woman 54 years old had her attention called to gastric symptoms and since the hard, immovable, moderately tender mass was detected in the pyloric region with the objective signs of pyloric obstruction, the diagnosis of carcinoma of the pylorus was made. In the drawing the fistula has been separated and the stones removed. Rupture of the gall bladder occurred in about 1.5 % of cases presenting themselves for gall bladder conditions.

ulcerative process proceeds too rapidly, the serosa gives way before it, can supply no protective adhesions and there results a general suppurative peritonitis, with ordinarily a fatal result. Localized phlegmons of the wall often begin in an ulcer. Perforation may also take place if a calculus is located in the cystic or common ducts.

In the wall of calculus containing gall bladders which were not too badly destroyed by severe inflammation, Aschoff and Otten found exceptionally numerous Luschka's ducts (p. 979), also marked formation of mucous glands even up to the fundus. Heterotopic gland overgrowth, eventually to cystic ectasia, may penetrate the wall to the serosa (see under chronic gastritis, p. 666). Bile is forced into Luschka's ducts, and if infectious, there results in the gall bladder wall the formation of foci of yellow granulation tissue consisting chiefly of large fat-filled macrophages, or abscesses, there, and in the vicinity of the ducts. The infection may quickly spread to the serosa and eventually cause a fatal peritonitis. Abscesses in the wall may perforate in either direction causing ulcers, without the influence of calculi. Calculi may be present in diverticulum-like enlargements of the ducts or may even have formed there (Ehrhardt, Lestchinski). The author has seen such cases. (See also under purulent inflammation of the gall bladder and bile channels in relation to calculi, p. 982.) Chiari and M. B. Schmidt saw aneurysm in the gall bladder in cholelithiasis leading to fatal hemorrhage into the bowel; Schnyder saw a fatal hemorrhage into the abdominal cavity from ulcerative errosion of an artery as a result of rupture of the gall bladder wall in the region of a second ulcer.

Constriction and Occlusion of Bile Channels

This may be caused by calculi, catarrhal secretions and catarrhal swelling in cholangitis, tumors, parasites, (ascaris lumbricoides and distomum), etc. Occasionally stenosis results from the contraction of scars in the healing of calculus ulcers, and thereby, in very rare cases, the common duct may be totally obliterated. Narrowing is also produced by the pull of peritoneal adhesions and bands, especially those subsequent to duodenal and gastric ulcers. When caused by tumors, it is chiefly by carcinomata, either of the bile ducts or the gall bladder itself, or by such as develop in the neighborhood, *i.e.*, primary carcinomas of the pancreas and the duodenum, and secondary carcinomas of the lymph nodes, of the portal vein, the peritoneum, etc. Carcinomas of the duodenum may be situated at the papilla, when icterus results, which may be intermittent as the tissue disintegrates and reforms.

Consequences of Occlusion of the Common, Hepatic and Cystic Ducts. (*a*) Closure of the common duct leads to bile stasis and icterus. Dilatation begins behind the closure and extends to all parts of the biliary system including the cystic duct and the gall bladder. According to Terrier and Courvoisier, the latter shrinks in chronic gall stone icterus, while in obstruction of the common duct from other causes, strictures, neoplasms, etc., it is usually distended. This had been substantiated from many quarters—Moynihan, lit. Rohde a.o.—but the author, as well as others, observed exceptions to this premise. In the earlier stages of bile stasis the liver as a whole is enlarged. The larger ducts may be cylindrically enlarged and become as thick as a thumb or occasionally as large as an intestine; sometimes the dilatation is varicose, or cyst-like. When

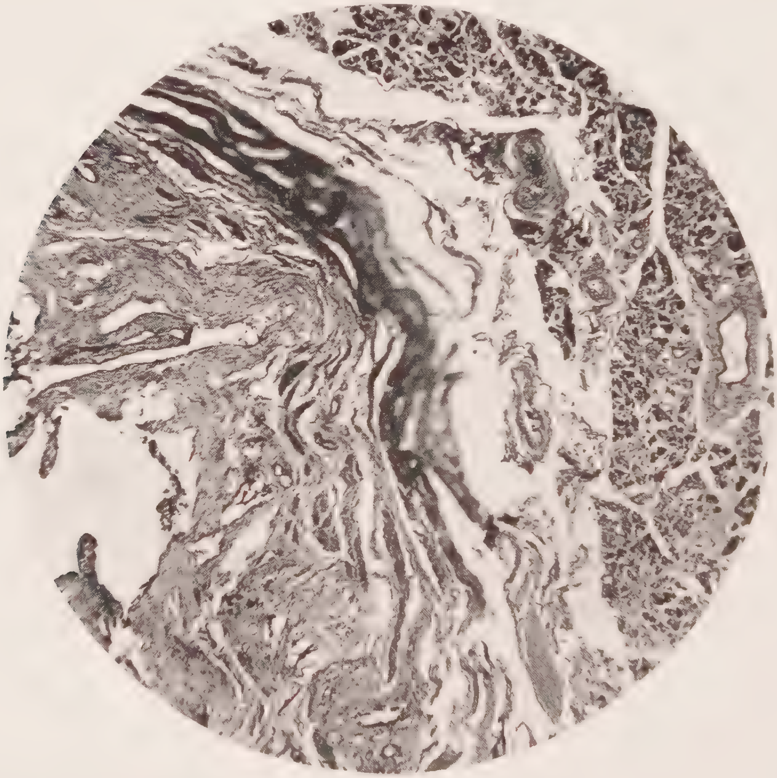


Fig. 492.—Section of the human ampulla of Vater. From a patient 48 years old who died of pneumonia. The section was taken as part of a study of this neighborhood. In discussing the causes of jaundice, spasm of the muscle of Oddi is frequently mentioned. Surgeons have the experience of opening the common duct and passing a blunt, bulbous-tipped probe toward the duodenum. When it meets with obstruction, if the tip of the probe is held with gentle pressure against the obstruction, after a time the obstruction is relieved, and the probe passes into the duodenum. This is assumed to be relaxation of a spasm of the sphincter muscle, but in some cases no amount of pressure will allow the probe to pass through. It is first necessary to begin with very small probes and gradually dilate the duct. If a portion of the pancreas is placed annularly around the duct, it is readily understandable that acute swelling or sclerosis of the pancreas will produce a stricture of the end of the duct which may come and go as the conditions vary in the pancreas. L. H.

the dilatation progresses to the smallest subserous bile channels, they may protrude on the surface like ampoules or bubbles, and occasionally rupture with consequent peritonitis, since under these conditions the bile practically always contains organisms (see cases of Karillon). The contents are either bile or a thick, lightly colored hydropic fluid. Hydrops of the biliary system—"white bile,"—from chronic obstruction by a neoplasm, etc., and accompanied by icterus and alcoholic stools is rare (Kausch, lit. Berg, Bertog). [See also Rous, P. and McMaster, P.D.; The Concentrating Activity of the Gall Bladder; J. Exp. Med. 34: 47, 1921; Physiolog. Causes for the Varied Character of Stasis Bile, ibid, 34: 75, 1921; The Biliary Aspects of Liver Disease, Am. J. Med. Sci. 170: 625, 1925. Also McMaster, P.D. and Rous, P. Hydrohepatosis, etc. Proc. Nat. Acad. Sci. 9: 19, 1923.—*Translator.*] The bile capillaries in chronic cases become clubbed and varicose; rupture is not uncommon. If the obstruction is permanent, necrosis and disintegration of the liver cells take place. Cholemia, *i.e.*, poisoning of the blood with all the substances which otherwise are excreted by the liver in the bile, causes the severe symptoms of icterus gravis which in many respects is similar to acute yellow atrophy of the liver. In this form of autointoxication numerous hemorrhages in the skin and the mucous membranes are characteristic. This hemorrhagic diathesis quite common in chronic icterus, may lead to hemorrhages into the greatly dilated gall bladder and bile channels and such a diathesis may in turn lead to grave and fatal complications in gall stone operations. In rare cases a massive calculus may be present without icterus. The author saw one exceeding the thickness of a thumb.

In animals after ligation of the common duct, a chronic connective tissue overgrowth, favoring cirrhosis is found (lit. by Tsunoda).

(*b*) Occlusion of the hepatic duct which may be caused by a stone, stricture, or a carcinoma, causes dilatation of the intrahepatic bile channels, and icterus, followed by cell necrosis as in (*a*). But if only one of the branches is permanently occluded, there follows atrophic shrinking of the affected part of the liver, as D. Nasse has demonstrated experimentally.

(*c*) Occlusion of the cystic duct usually causes hydrops of the gall bladder (cholecystectasis). If this duct is plugged, no fresh bile enters the gall bladder, the specific biliary contents are soon absorbed by the lymph vessels of the organ, and a clear fluid collects, secreted by the mucosa, stretching the gall bladder more and more. If catarrh of the mucosa is present in addition, the hydrops may assume enormous size. Then the gall bladder protrudes from under the liver as a large tense tumor which can be palpated as a hard globular mass through the abdominal wall. The contents are either pure mucinous material, white, and clear, or more serous, thinner and yellowish. Opinions still differ concerning the inflammatory origin of hydrops (Aschoff, Sprengel). Chronic hydrops is usually sterile. The mucosa becomes smooth, devoid of its folds, its epithelium is flattened and undergoes fatty degeneration. The muscular elements soon disappear from the wall and are replaced by fibrous tissue, the inner surface becomes tendonous and snow-white, the wall is either thinned to paper thickness, or becomes thickened; occasionally it looks like the icing over a cake.

Frequently a pure cholesterin calculus, (occlusion stone—Aschoff), is found in the neck of the gall bladder, and is said to favor infection, and the formation of ordinary calculi. But cases are seen such as one of the author's in a 62 year old woman, in whom a gall bladder the size of a goose-egg contained clear hydropic fluid and numerous ordinary gall stones from the size of a pea to a hazel nut. An irregularly globular one was tightly impacted in the neck of the gall bladder (see also Kretz).

Cases of hydrocholecystitis in duodenal catarrh without cholelithiasis are of interest. The author saw such a case in a man 50 years old with icterus and marked fat necrosis of the pancreas showing an unusual mechanism occluding the cystic duct causing icterus. The duct was kinked at an angle against the globular, distended neck of the gall bladder which was of the size of a fist. It resembled the kinking of a ureter seen so frequently in hydronephrosis. The lumen was perfectly free after the kink was straightened out. The globular mass had interfered with the common duct as well as with the duct of Wirsung which was also distended. A small mucous polyp at its orifice contributed to the obstruction. Nowhere were there scars or signs of a previous cholelithiasis. The liver was smaller than normal and grass green.

Obstructive jaundice from torsion of the gall bladder is quite rare (see p. 979); the gall bladder, the size of a child's head was twisted several times and hanging down in the right inguinal ring. Hemorrhagic infarction changed it to a heavy tumor (Mayer).

If the gall bladder is infected by way of the bowel, and the cystic duct occluded by a calculus, empyema of the gall bladder or a severe phlegmonous destructive inflammation develops, since by occlusion and retention the virulence of the bacteria increases (see Sprengel). The gall bladder may reach a size beyond that of a child's head. It is thought that an empyema may change gradually into hydrops by absorption and granulation (see Kummell, lit.).

In other cases, after occlusion of the cystic duct, the gall bladder atrophies, and usually contains a grumous mass consisting of calcified thickened secretion.

For gall bladder dilatation from obstruction of the common duct, see p. 998.

Edema of the mucosa and submucosa must not be mistaken for hydrops. It is a pure mechanical congestive edema seen especially in heart lesions, but also in tumors. It may have an inflammatory origin in conjunction with ulceration. The wall of the gall bladder reaches the thickness of a finger, becomes jelly-like, pale-yellow or whitish, and the opposing walls almost touch. The edema may also be confined to the wall, without affecting the mucosa.

Specific Infectious Granulating Inflammations

In congenital syphilis, fibrous overgrowth and gumma formation may occur in the gall bladder and the vicinity of the bile ducts, causing possible stenosis and obliterations. At times there are extensive, firm, tube-like thickenings. If icterus follows, these cases often prove fatal (see under liver, p. 940).

Tuberculosis rarely affects the gall bladder. Sometimes it is in conjunction with calculus formation. Through destruction of tubercles, chronic, round, pointed or star-shaped ulcers are formed. Occasionally there is extensive caseation (cases of Kisch, Beitzke), or perforation. Deyche describes clinical primary tuberculosis of the gall bladder with calculus formation. In acute tuberculosis, Simmonds (lit.) saw tiny circumscribed necroses of the mucosa, containing the bacilli. Caseous lymph nodes in the hilus of the liver can cause obstructive jaundice.

> **Translator's Remarks.**—Rankin and Massie report a case of primary tuberculosis of the gall bladder followed by tuberculous peritonitis. Ann. Surg., 83: 800: 1926. The translator encountered but one case in the many gall bladders examined—woman, 40, several calculi, one caseous nodule in fundus, histologically definite, uneventful operative recovery.

In typhoid fever, the specific bacilli are found in the gall bladder contents, but cause no changes, as a rule. They may penetrate the wall, however, and cause diffuse extensive inflammation, phlegmons and ulcers (see p. 983, Chiari), but this is rare. Necroses as mentioned on p. 982, are still more rare. Ichoric suppuration probably occurs only in the simultaneous presence of anaerobic organisms (see Eug. Fraenkel). The danger of perforation is constantly present, but rarely occurs. The author saw three cases with perforation; in two, calculi were present. The typhoid cholecystitis doubtless gave the impetus to primary stone formation in these cases (see p. 990). In other cases, calculi favor the invasion of typhoid bacilli. With the greater tendency of women to cholecystitis, they must naturally have the greater number of permanent carriers included in their sex (see p. 783). The operative removal of the gall bladder usually stops the elimination of the bacilli (see Grimme-Fromme).

Glanders, leprosy, actinomycosis (Mayo-Robson) are rare.

Tumors of the Gall Bladder and Large Bile Ducts

(Tumors of small bile channels were discussed under liver, pp. 959 to 965.)

Benign Tumors are Rare. There occur tuberous fibromas and papillary fibro-epitheliomas, the latter usually in old people as small, grayish-red, soft, papillary growths eventually becoming encrusted. The author saw them in women, one 70, the other 57 years old, as small isolated pedunculated tumors in the otherwise unchanged gall bladder, but also in a woman 37 years old as numerous fringed tabs in a large inflamed calculus-containing gall bladder, (see also Molle, Schoenlang, Sand and Mayer, lit.). It is differentiated from the very rare papilliferous carcinoma by its remaining confined to the mucosa. In some animals, these papillomas become very large, and form systems of closely packed excrescences like uvulae. There is such a preparation from a horse with cholelithiasis in the museum in Breslau (for carcinomatous transformation of gall bladder papillomas see Pels Leusden, Hruska, lit.). Sometimes in cholelithiasis there is a very irregular hypertrophy of the mucous glands, and Ikeda describes a fibro-adenoma of the gall bladder which he considers derived from Luschka's ducts. We have seen cyst-adenomas but rarely, and then usually of small size which bulged spherically or hemispherically from the serosa or from the wall. Barberio described a cyst-adenoma of the hepatic duct. Volmer, and Mertens and Stahr described the very rare adenomyomas of the common duct.

Of malignant tumors only carcinomas are frequent; sarcomas are very rare. The literature mentions 13 **sarcomas,** 10 accompanied by gall stones. Histologically, they are usually of the spindle cell type with giant cells; one was seen by the author in a 52 year old woman with cholelithiasis (published by Iwasaki). In a second case in a woman 59 years old with cholelithiasis, published by Stickdorn, the author found cartilage, an observation made in but one other case, that of Bayer. Women are afflicted twice as frequently as men; the age varies from 45 to 68 years (lit. by Landsteiner, Parlavecchio, Bayer, Hotes, Jaffe). Landsteiner saw a squamous cell carcinoma and a myxosarcoma in the same specimen. Shepherd described a primary melanotic sarcoma of the common duct.

Carcinoma of the gall bladder occurs mostly in older individuals and more frequently in women; generally there is an accompanying cholelithiasis. According to the observations in Breslau, it occurred in 5%, according to those at Basel 5.19%, according to Gottingen, over 7% of carcinoma cases autopsied. It very frequently starts at the junction of the fundus and neck; in other cases it begins in the fundus with perhaps a somewhat more favorable prognosis. The tumor then enlarges either by diffuse infiltration or as a nodule. The free surface toward the cavity of the gall bladder usually ulcerates. Frequently the tumor extends into the liver parenchyma as a confluent nodule; one seen by the author in a

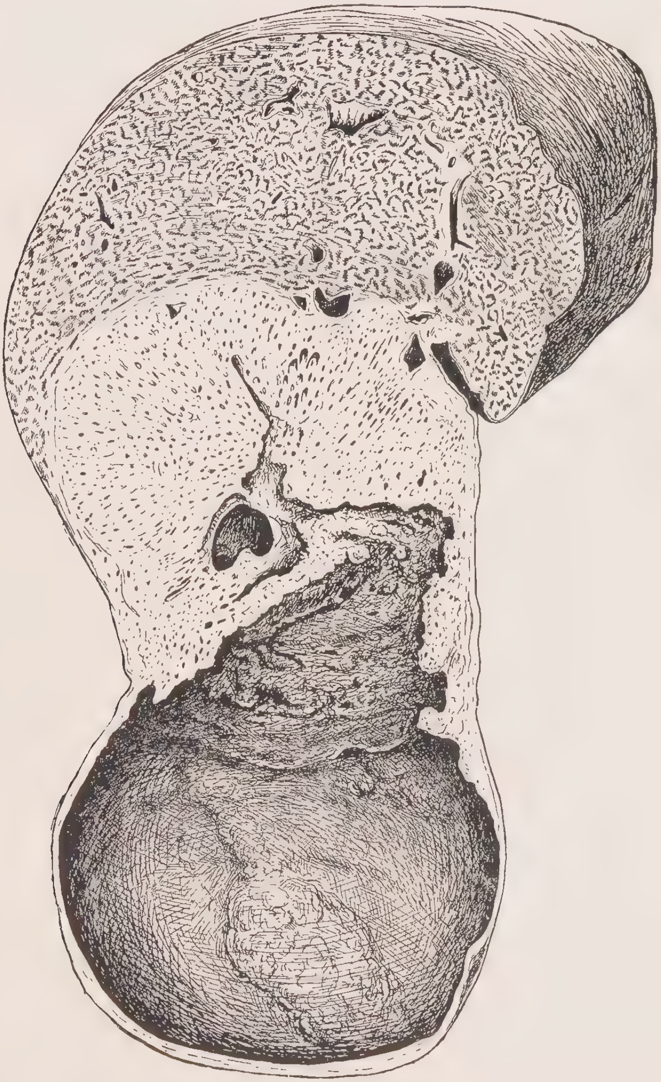


FIG. 493.—Suppurating carcinoma of gall bladder, extending into the depth of the liver. C, carcinoma; G, gall bladder, markedly dilated and thickened, contained numerous gall stones; S, groove due to tight lacing; L, liver, perpendicular sect; view of right side; ¾ nat. size.

woman 47 years of age attained the size of a man's head. Less frequently there are scattered metastases in the liver.

The gall bladder is usually distended, hydropic, or filled with pus and contains calculi remarkably often. In very rare cases, the entire wall is infiltrated forming a tumor the size of a fist or larger, in the center of which is found a stone filled cavity, with usually very little gall bladder wall remaining. But the carcinomatous gall bladder may also shrink to a mass the size of a bean, with its cavity containing calculi. The author saw a gall bladder in the walls of which were 3 prominent beet-like adenocarcinomata apparently independent, but in reality connected by infiltration in the thickened wall. Sometimes, secondary tumors in the mucosa or within the gall bladder wall are seen; when these grow in the cystic or common ducts, stenosis results with possible deep jaundice. This dissemination is via the lymph channels. If the wall shows whole chains of nodules or a diffuse infiltration over extensive areas, it is evident that metastases to the portal nodes are common. Scattered prominent nodules in the mucosa may simulate implantation. The author saw a gall bladder carcinoma in a woman 50 years old with gall stones and a most pronounced furrow from excessive lacing, in whom the duodenal papilla of the common duct showed a small carcinomatous nodule and the caecum a carcinoma the size of a fist. The duodenum may also become stenosed. The transverse colon may become adherent by carcinomatous infiltration and, as seen by the author, perforation and fistulae may occur. In a woman 66 years old, there was simultaneous fistulous perforation through the umbilicus.

During life, even a large nodule may escape detection on account of its hidden growth. Often, instead of the tumor below the abdominal walls, the dilated fundus of a tensely filled gall bladder is felt. Many cases are clinically masked under the picture of cholelithiasis. Others remain unrecognized because of secondary intestinal stenoses; metastases of Douglas especially dominate the picture (see the works of Dann and Schwietering).

Different Forms of Carcinoma of the Gall Bladder. Metastases.—Carcinoma of the gall bladder occurs as a cylindrical cell or round cell tumor with their subdivisions, scirrhous, colloid, etc.; rarely, epithelial metaplasia leads to a squamous cell carcinoma (lit. Deetz, Firket Nicholson and others). It starts from the lining epithelium or the mucous glands (see also lit. by Senger). Both squamous cell carcinoma and adenocarcinoma either as two separate growths or one with two cell types from the beginning, are known to occur. It is also possible to have squamous cells metamorphose into cylindrical cell carcinomata (Deetz, lit., Monckeberg, Buchmann). Simmonds calls them "mixed" carcinomata. Villous carcinomas are very rare, but the author saw one in a 70 year old woman which arose in the fundus as a red papilliferous tumor the size of a cherry. The basal layer of the villi was composed partly of solid masses of epithelium and partly of invading acini-like structures. The deep layers of mucosa were heavily infiltrated by alveoli of large cylindrical cells. There were no calculi; a secondary diffuse carcinoma of the liver brought the weight of this organ to 3200 gms. Spongy, cauliflower-like carcinomas are rare, but may distend the gall bladder to the size of a fist. Indeed some as large as a man's head have been observed; a case of Michaux's was taken clinically for an ovarian tumor. Wieting and Hamdi described a melano-carcinoma. In the scirrhous variety, the tumor may be diffuse, but not excessive in size and rather resembles a chronic, fibrous, indurating and thickening inflammation, but metastases seldom spare the adjacent lymph nodes. Sometimes, the peritoneum is infiltrated by a diffuse scirrhous growth (p. 878).

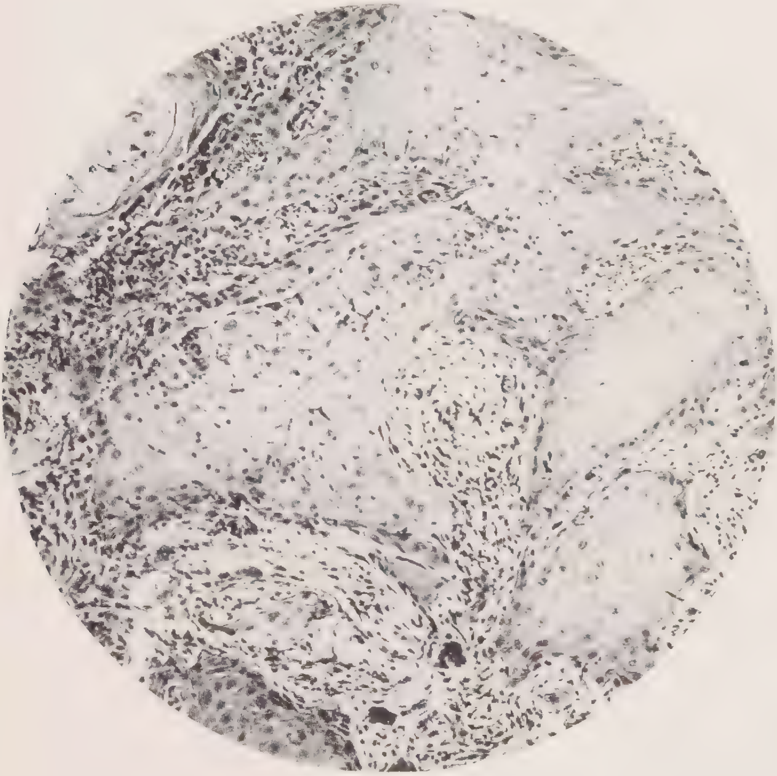


Fig. 494.—Squamous cell carcinoma of the gall bladder. From a patient 62 years old. In ten carcinomas of the gall bladder, this type occurred once. It was present in an organ diseased for many years and containing stones. It is a type of interesting reversion of cell structure encountered occasionally as a suggested result of long continued chronic irritation. Keratinized centers of some of the bodies are plainly in evidence. × 120. L. H. #18900.

> **Translator's Remarks.** Cornifying squamous cell carcinoma was encountered by the translator twice in fourteen specimens; both gall bladders contained stones. Both patients died of metastases in less than a year after operation.

In **colloid tumors,** which may diffusely infiltrate the entire wall, the peritoneum is often quite extensively involved (p. 878). Curiously enough both ovaries are frequently filled with metastases. The soft cylindrical cell carcinoma forms a large white tumor with its greatest mass penetrating the liver above and posteriorly, while the free surface in the cavity of the gall bladder is ulcerated. Frequently, massive nodular metastases occur in the peritoneum, the lymph nodes, mesenteries and in the gastro-colic ligament. They may be quite vascular, with degenerating centers so that fluctuating, cystic masses the size of a fist or larger, are not uncommon. The secondary then far exceeds the primary tumor in size. According to the statistics at Basel, 39.5% of cases showed metastases to the liver.

Changes in the Adjacent Vessels.—To the purulent degeneration of a carcinoma of the gall bladder may be added a suppurating pyelophlebitis which involves all large roots of the portal vein. Thrombosis of branches of the hepatic veins with its consequences is not rare. Even a thrombosis of the vena cava may extend to the auricle.

Etiology.—According to the data at Basel, gall stones are found in 86% of cases of gall bladder carcinoma. There is therefore justification in assuming that cholelithiasis acts as a chronic irritant and analogous to other regions in which chronic irritation is present, stones may favor the development of carcinoma if it is shown that the calculi were present previous to the beginning of the carcinoma. This supposition is rendered more probable if there is found simultaneously, an old, well marked constriction or furrow from excessive lacing and the scars of healed pressure ulcers caused by calculi. At times the starting point may be in the scars themselves, especially of the scirrhous type which are poor in cells. But a definite decision is difficult, since calculi may form in six months, and thus be no older than the carcinoma. But occasionally true calculi of secondary formation are seen, *i.e.*, incrustations of tissue detritus of the carcinoma itself, (see under secondary tumors). Corresponding to the fact that cholelithiasis is found in women more frequently than in men, gall bladder carcinoma is also more prevalent in that sex, according to the statistics of Basel, (56 cases) 87.5%, and of Gottingen 89.62% (in 106 cases), (see Diss. Feldner and Schwietering). The tumor is usually found in older people; according to the statistics from Basel, 60% of cases occur between the ages of 50 and 60 years. The author saw a carcinoma in the neck of the gall bladder, with calculi in a 95 year old woman. The local extension was slight, but infiltration had caused stenosis of the papilla, severe icterus, metastases to the peritoneum with stenosis of the bowel. Probably this is the oldest case on record. Haberfeld mentions in his work (Z. f. K. VII, Vol. 1908) as the most aged case, a man of 93, (observed by Riedel).

The youngest individuals in whom the author found gall bladder carcinoma were: a soldier 25 years old; gall bladder: thickness of small finger, contents turbid mucus; diffuse infiltration of wall, scirrhous adenocarcinoma, no calculi, constricting metastasis of Douglas, carcinoma extended to the liver, metastases to portal lymph nodes (published by Schwietering). In a man of 32 years, carcinoma in neck of gall bladder, calculi, empyema of gall bladder, liver 5.5 kgs., many abdominal lymph node metastases, etc. In a man of 33, carcinoma in fundus, no calculi, metastases to peritoneum, liver and retroperitoneal lymph nodes; also 2 women each 35 years old with gall stones. In the latter, an immense hydrops of the gall bladder the size of a fist was found. The neck showed calculi and an ulcerating carcinoma with metastases in the liver; excessive loss of weight in last 3 months. The first symptoms of hydrops 7 years before. Liver showed lacing furrow.

Carcinoma of the large bile ducts usually causes stenosis; it is rather rare, and does not occur more frequently in females than in males; calculus formation is usually absent. This form leads frequently to enormous proximal dilatation of the bile ducts and, as a rule, causes deep icterus and cachexia. We deal with carcinoma of the **common duct** (lit. by Miodowski, Morian, Konjetzny), or of the **cystic duct** (rare, see Chini) or of the hepatic duct which may be situated intrahepatically and is classed by many among the primary carcinomata of the liver. The favorite locality is the junction of the three large bile ducts and the segment of the hepatic duct from this point upward to its bifurcation (lit. by Rocco, I. Diss. Basel, Lapointe and Raymond, Borelius, Pallin). The tumor form, varying in size from a pea to a hen's egg, but usually small, can be differentiated from the infiltrative form, the latter usually appearing as a hard, annular, scirrhous adenocarcinoma of quite limited extent, easily overlooked, but which at times infiltrates the wall for some distance, or, as secondary carcinomas sometimes do, grows in a retrograde direction in Glisson's capsule or more rarely as villi within the lumen, thus forming small secondary nodules. They often continue to the liver, more rarely to the pancreas, in which case stasis of secretion and fat necrosis may follow. The carcinomas of the cystic duct frequently extend by continuity to the gall bladder. These carcinomas arise from the epithelium of the bile ducts or their mucous glands. Even mucoid carcinomas are seen.

Consequences.—Bile stasis with enlargement of the liver is frequent, while cholangitis following infection of dilated bile channels is rare according to Devic and Gallavardin; dilatation of the gall bladder occurs in about half the cases according to Miodowski. Metastasis is often absent, even in the regional lymph nodes, *i.e.*, portal and retroperitoneal, but has been known to assume immense proportions, especially in the liver. The author performed an autopsy on a woman 59 years old, and found a small hard carcinoma, causing stenosis, so that only a very fine probe could be passed; it was situated in the left main branch of the hepatic duct and there was enormous infiltration of regional lymph nodes, which reached the size of two fists, causing narrowing of the common duct and the duct of Wirsung; the pancreas itself was closely surrounded by tumor masses and extensive fat necrosis had occurred. The author also saw metastases to the lung following invasion of the thoracic duct.

Secondary carcinomas of the large bile ducts may develop by extension from a carcinoma in the neighborhood, pancreas, duodenum, stomach, or from a gall bladder carcinoma. The author saw an unusual case in a 68 year old man in whom a mushroom-shaped carcinoma of a round cell type, arising in the fundus of the stomach, had produced carcinomatous masses from the porta hepatica along the bile ducts, enclosing them; it then extended along the small shrunken gall bladder and supplied it with a white capsule, 1.5 cm. in thickness giving the impression of a primary tumor of the gall bladder, or bile ducts. Very rarely they start from a metastatic nodule in the liver which may happen to extend into a large bile channel (see observation of author, p. 822).

Secondary tumors of the gall bladder are very rare. Pigmented sarcomas occur. In a 46 year old man who had a sarcomatous naevus on his back, the author saw 12 melanotic sarcomas of the size of hempseeds, and in a man 48 years old with melanotic sarcoma, one year after bulbar extirpation for a choroideal tumor, several nodules, pinhead-size, were found in the mucosa. True metastatic carcinomas occur, although rarely, (see observation on p. 246) and, as a rule, no calculi are found, *i.e.*, according to Siegert only in 15 to 16%, while in primary carcinoma, they are found in 95% of cases.

Parasites.—Echinococcus infestation of the gall bladder is quite rare, appearing as a multilocular tumor in which calculi may be found, as in the case of Huber-Zenker, or as an hydatid either single or as a mother cyst with its daughter cysts in the gall bladder. They may reach the size of a child's head (lit. by Chiari). For perforation into the bile ducts, see p. 977.

Distomum Felineum.—Opisthorchis felineus, Kazennegel, about 1 cm. long × 2 mm. wide, inhabits the bile ducts; it occurs in cats and also in dogs. It was first observed in Pisa by Rivolta, afterwards in Siberia and eastern Prussia. Modes of infestation: ingestion of raw or insufficiently cooked fish. In man, single or numerous specimens are found in the bile ducts, but they also occur singly in the bowel and pancreas. The consequences are unimportant, or when larger numbers are present, jaundice, cholangitis with necrosis and polypoid overgrowth, cirrhosis of the liver, and what is of special interest, carcinomas of the intrahepatic bile channels, or of the head of the pancreas, which possibly develop from chronic inflammatory changes and primarily benign epithelial overgrowths.

See p. 852 concerning ascaris lumbricoides and its rare intravital invasion of the bile ducts.

Icterus

Obstructive or Mechanical Icterus (**Absorption Icterus**).—When the outflow of bile produced in the liver is prevented, it is reabsorbed by the hepatic lymph vessels, carried to the thoracic duct, and thence into the general circulation, (cholemia); it soon appears in the urine (choluria, bile pigments and bile salts). Icterus means saturation of the tissues by bile pigment mostly bilirubin or biliverdin, at first with the pigment in solution, later, with granular and partly crystalline precipitates.

While the presence of hematoidin crystals which appear as red rhombic plates or as fine, golden yellow needles has been long recognized in the icterus of the newborn, recently, this has also been demonstrated in adults (Dunzelt).

Hematoidin derived from hemoglobin is identical with bilirubin. Biliverdin is formed from bilirubin by oxidation. Urobilin probably formed from bilirubin in the bowel by reduction, may sometimes appear in the urine, urobilin-icterus, but the icterus in those cases is likewise produced by bilirubin. It is well known that bilirubin can be produced outside of the liver in hemorrhages and hemorrhagic exudates, and a slight general icterus occurs in such circumstances (see lit. by Lepehne).

Opinions are still divided as to the path by which bile reaches the general circulation just as they are in reference to the hepatic lymph channels themselves. Repetition of the experimental investigations of Fleischl, Kufferath and v. Frey who studied the flow of bile in the thoracic duct after ligation of the common duct, has shown that icterus develops, even after ligation of the biliary and thoracic ducts (D. Gerhardt). The entrance into the blood must therefore be direct, and it was concluded that the direct route was chosen if the lymph route was blocked. Browicz and others, however, do not share this opinion, but believe that absorption by the lymph channels occurs about the larger intrahepatic bile channels, while intraacinar absorption occurs only by way of the blood (see also remarks on the anatomy, p. 1013).

Hijmann von den Bergh's interesting experiments led to the theory that there are two types of jaundice corresponding to a prompt or a delayed diazo reaction of bilirubin in the blood serum. The sera from cases of obstructive jaundice give a prompt reaction, while those from hemolytic icterus and similar conditions, in which it is assumed that bilirubin does not reach the blood via bile stasis and absorption, but in some other way, give delayed reactions. For this reason, Lepehne speaks of "obstructive bilirubin" and "functional bilirubin." In this detail which is highly important in icterus, the terms "icterus with bile stasis" or "mechanical icterus," and "icterus without bile stasis" or "dynamic icterus" are often used. But we cannot enter further into this discussion (lit. by Lepehne).

H. Eppinger points out that the possibility of pigment absorption from the gall bladder must not be ignored (see p. 999, the well known absorption of bile in hydrops).

It is the yellow color of the skin and sclera which is most spectacular. The latter may become green—icterus viridis—and after longer duration may change to greenish gray—icterus melas. The urine varies from a deep yellow to brown. If obstruction is complete, the feces are pale, clay-colored, grayish-white, fatty, shiny, unguent- or putty-like in consistency, and thanks to the insufficient fat digestion and the abundance of fatty acids and soap needles, the odor is fetid. But pure gray feces may have contained bile if the bilirubin has been reduced completely to urobilirubin which has no color (leucourobilin; see Naunyn). The liver is yellowish green to dark green according to the degree of jaundice. The kidneys more than other organs are intensely stained a grass green. The blood plasma contains bilirubin, and this discolors the intima of the vessels and the cardiac valves, especially the latter, even in mild icterus. Transudates assume a golden yellow to greenish brown color; even the sweat may be pigmented, but other secretions such as tears, saliva and mucus are not colored; neither are cartilage, the cornea, muscles or specific nerve substances. The ventricular fluid is frequently colorless, (Schmorl, see also Askanazy), while the cerebrospinal fluid is yellow. Exceptionally, there is intensive yellow discoloration of the brain in the icterus of the newborn, as was seen by the author in confirmation of Schmorl's findings. It is at times diffuse, at other times blotchy, electively confined to the nuclear areas such as the lenticular nucleus, corpus striatum and around the aqueduct of Sylvius; in these cases the ganglion cells take the bile stain. See Beneke, Hart, Pfaeltzer (who considers it an infection), for this nuclear icterus. v. Gierke found erythroblastosis associated, (see p. 240), a condition seen also by the author in a very pronounced case, in which extensive hemorrhages in the lungs and kidneys were also present (Palm). The bodies of icteric cases like those with sepsis, decompose rapidly.

Icterus may be due to (*a*) general bile stasis, the cause of which was discussed above, *i.e.*, conditions narrowing or occluding the large bile ducts, (*b*) to partial obstruction in the liver itself as from pressure exerted on minute and larger bile channels in hypertrophic or common cirrhosis, which may lead to ectasias and ruptures; intrahepatic calculus formation, or tumors; or, as seen by the author, pressure exerted from an intrahepatic aneurysm of the hepatic artery. "Emotional" icterus is considered due to cholangiospasm and if this continues for some time the mechanical factor of so-called bile thrombosis may be added (Umber).

The Microscopic Picture of the Liver.—In cases of long standing, the distended bile capillaries appear as clubbed, varicose, globular or branching, yellowish green, shining structures, forced between the liver cells. Sometimes a network appears as in an injection preparation, especially in the centers of lobules. Some liver cells are stained diffusely, others are pigmented by droplets, granules and needle-like crystals of bile pigment. Later, the bile capillaries are plugged by solidified bile, the so-called bile thrombi of green or greenish black color. The distended tubules of the liver cells are also filled with bile (see p. 1014). Green and yellow granules may be embedded in the renal epithelium.

Gmelin's Reaction for the Demonstration of Bile Pigment in Sections.—Potassium hydroxide solution is placed on a fresh section, and after a short time is washed in water. Then strong nitric acid containing nitrites is added and the transition of color from green through blue, violet to red is observed.

Continued bile stasis then leads to necrosis of the liver cells from the action of the bile in the protoplasm (Gerhardt-Ogata) (see also necrosis of renal epithelium in grass green kidneys). This occurs in multiple foci which attain the size of a millet seed; they are rounded, light, pale yellow and accompanied by a productive connective tissue inflammation (see biliary cirrhosis, p. 933). The addition of infection from the bowel is followed promptly by severe inflammatory processes in the bile channels which in turn lead to purulent cholangitis, pericholangitis and abscess formation (see p. 920). Acute atrophy, *i.e.*, acute disintegration of liver cells, has also been observed after simple obstructive jaundice.

The bile pigments and bile acids are carried into the blood and in part excreted by the kidneys which show the consequences in the epithelium (see under kidneys). Part is excreted by the sweat glands, but another part is returned again to the liver and again excreted in the bile, and so on. If the obstruction is removed,—when, *e.g.*, a plug of mucus closing the papilla is expelled—a large quantity of bile flows suddenly into the bowel.

Here the pigment is reduced to hydro-bilirubin (urobilin) with the help of bacteria. In the intestine of the fetus, therefore, where no bacteria are present, unchanged bilirubin is found. In the yellow intestinal contents of the nursing baby also, there is unchanged, or only slightly reduced bilirubin. By the oxidation of bilirubin, biliverdin is formed. A part of the urobilin is reabsorbed into the blood from the bowel; a part of this is again taken up by the liver and excreted in the bile; another part is directly eliminated in the urine. Urobilin is identical with stercobilin, as prepared from normal feces (details by Weintraud). As jaundice disappears the urine behaves thus: bilirubin disappears and urobilin appears in abundance (urobilinuria), as the flow of bile into the bowel is reestablished (for details, see Fischler).

Jaundice from Bile in the Blood without Mechanical Interference with the Bile Flow (Diffusion Icterus).—In obstructive icterus, a mechanical factor is the chief cause of the presence of bile in the blood; in another type of icterus no such cause can be demonstrated anatomically, *i.e.*, there is no mechanical obstruction of the channels and the feces contain pigment. Therefore, in contradistinction to mechanical icterus, the term "functional" or "dynamic" icterus is used.

Thus we see a slight discoloration of the sclera and skin when hemoglobin and its derivatives enter the circulation in large quantities, *e.g.*, from a massive extravasation of blood in a ruptured ectopic pregnancy, in traumatic hemothorax, etc.

It has been mentioned, (see p. 1009), that general icterus is rare in these cases, and Naunyn insists upon a separate classification. The blood serum usually contains abundant hematin, which was formed in the hemorrhage, but rarely shows a high bilirubin content (in ectopic gestation, see Schottmuller, lit.).

When many red blood cells are destroyed in the circulating blood, or when the hemoglobin separates out in clumps or in solution, or when the blood already contains extrahepatic bilirubin in large quantities as from the spleen, the blood serum then is so saturated with hemoglobin or its derivatives, that in spite of increased activity of the spleen and kidneys, and increased production (hypercholia), of a very thick bile rich in pigments, (pleiochromic), the total quantity cannot be excreted in the normal manner and icterus appears. In other types of hemolytic icterus, the blood serum contains much bilirubin and the liver cannot accept and excrete it because of functional insufficiency; therefore it remains in the blood and causes icterus. In certain other cases it is assumed there is secondary bile stasis in the bile capillaries with reabsorption, as in toluylendiamin-icterus (see Lepehne, lit.). Thus, many conditions lead to dynamic icterus, such as hemolytic poisons, among which are arsenuiretted hydrogen, toad stool poison, (helvalluvic acid, phallin?), toluylendiamin, so important in studies of icterus, nitrites, certain hydrochloric acid salts, pyrogallol, anilins, (antifebrin), phosphorus among the toxic causes. To the same class belong the infections, such as pneumonia, typhoid fever, scarlet fever, Weil's disease, etc., when they are known as infectious icterus. The pathogenesis is by no means uniform, and there are many opinions in regard to it, (see p. 1016 in reference to the theories of hemolytic icterus).

(See p. 192 in reference to familial hemolytic icterus; for Weil's disease, infectious icterus, see p. 1019.)

In cyanotic icterus—the icterus of cardiac disease—Naunyn thinks that local causes, such as capillary cholangia and congestion, are developed; at least, in some cases there are numerous bile thrombi (see also Lepehne).

The jaundice of pneumonia is thought related to destruction of erythrocytes in the affected lung and thus of a hemolytic-pleiochrome origin, but there is also functional injury to the liver cells (see Lepehne, lit. Roccavilla). Naunyn believes there is mild cholangitis (for methemoglobin formation by pneumococci, see Schnabel).

Anatomical Remarks.—Several points must be touched upon to understand the argument in the question of how bile, *i.e.*, bile pigment, enters the blood. According to Kupffer and others, the intracellular capillaries begin as "secretion" vacuoles with button-like ends within the liver cells, from which radiate the most minute intracellular secretory channels which envelop the nucleus, (Browicz, Nauwerk), and, according to Browicz, enter it. In chronic bile stasis these are filled with brown and yellowish green masses. Then there is supposed to be a close intimacy between liver cells and blood capillaries of such type that the intracellular reticulum can be injected from the blood vessels (Fraser and Nawerk). Further, Browicz believes there are minute capillary tubes formed during bile stasis which connect the liver cells with the cells of the capillary walls. He saw the latter bile stained, and argues that bile may be excreted into them from the liver cells, at least under pathological conditions. A possible physiological function of these intracellular pathways is to allow entrance of nutriment from the blood into the liver cells, and of red cells themselves, while intracellular bile channels serve as a means of exit (Browicz). Although Schaffer verified in injected rabbit livers, Browicz's findings in human livers, Holmgren questions their significance. Furthermore, Arnold (lit.) denies the existence of intracellular canaliculi and interprets them as granules or granule-chains. Noel Fiessinger (lit.) thinks that Browicz's conception is based on unsuitable pathological material; Eppinger, by using special staining methods, describes short lateral prolongations of the intercellular bile capillaries extending into the liver cells (intracellular bile capillaries), which have a tendency to be directed toward the blood vessels. Ciechanowski evolved another method to show the same thing. But these prolongations never reach the blood capillaries, and bile and blood capillaries are always separated by liver cell protoplasm. The blood capillaries are said to be enveloped by a system of fibres, with interstices similar to those in connective tissue, but there are no lymph capillaries with separate walls. Browicz, nevertheless, clings to his opinion in spite of these investigations. When the lateral buds of bile canaliculi are distended enough by stasis, they rupture and with them, the liver cells, whereupon bile passes into the interstices of the fibrous tissue network surrounding the blood capillaries, from which it enters the lymph stream and the blood by way of the thoracic duct. Furthermore, the bile is "thrombosed," already described by Affanassiew, and clumps of debris plug the bile capillaries like corks, thus furthering the stasis and tearing of liver cells. There are many opinions concerning

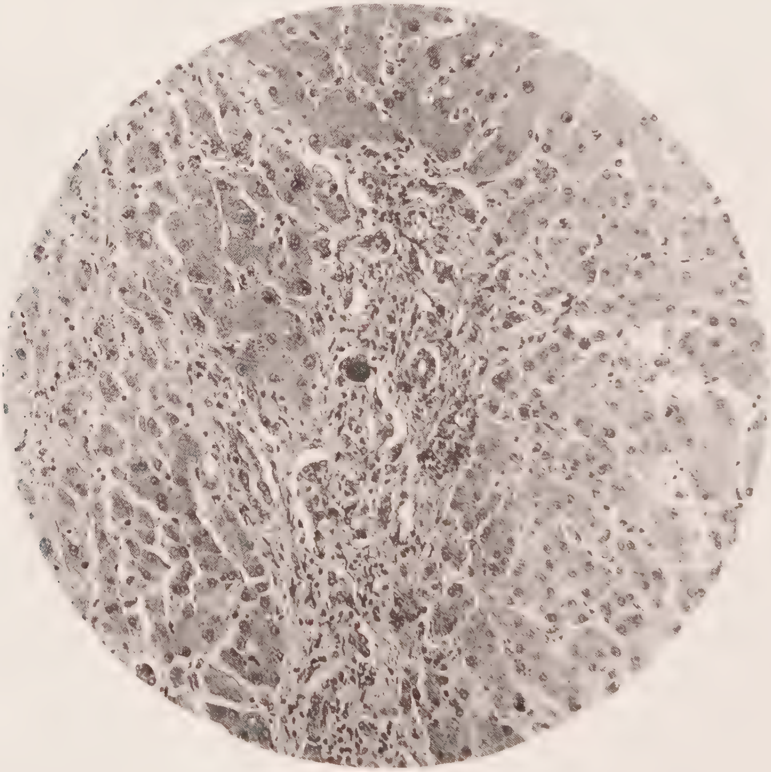


FIG. 495.—Bile thrombus in a small bile duct. The rounded black figure in the center is the "thrombus." These are present in all cases of jaundice. They often tend to assume geometric shapes such as four or five pointed stars or triangles, etc., conforming to the shape and branching of the ducts in which they are deposited. Their color in the H. and E. preparation is yellow brown. × 74. L. H. #90.

the origin of these bile thrombi; some state that the bile is thickened, others that it coagulates, protein impregnated with bile pigments is precipitated, etc. Lepehne believes they express toxic injury to liver cells, resulting in a qualitatively changed bile secretion. At any rate, thrombus formation occurs without the necessity of such mechanical factors as occlusion of the large bile ducts (see hemolytic and hematogenous icterus, p. 1016).

How does the icterus develop in these cases? Formerly, the term hematogenous icterus was used to mean a change of hemoglobin into bilirubin in the blood itself. Virchow, as we know, was the first to demonstrate that this can occur outside the liver (see p. 1009), but the bile acids were not considered; a fact also true of the modern theory of hematogenous icterus (see p. 1016). Bile acids, as Naunyn first demonstrated in septic jaundice, are increased in the urine of many icteric cases, as well as in the physiologic bilirubinuria of the dog (see Naunyn). But the well known investigations of Naunyn and Minkowski established in birds (geese and ducks), that jaundice, which otherwise always appeared after the inhalation of arsine, did not follow when their livers were removed, and thus the theory was formulated that icterus does not develop without the intervention of the liver.

In cases in which there is no gross obstruction, *i.e.*, after poisoning with hemolytic agents, such as arsine, toluylendiamin, etc., Stadelmann then thought that a thick bile, rich in pigments is formed (pleiochromic), too viscid to flow through the minute biliary canaliculi (icterus pleiochromicus); but this conception never met with general favor, and Naunyn quite recently repeated that there is no icterus caused purely by excess of bile pigment formation, that indeed pleiochromy leads to icterus only because of a capillary cholangitis (see below).

Parapedesis of bile, a theory first promulgated by Minkowski, was now considered in opposition. Minkowski assumed that the liver cells secrete in two directions, externally toward the bile channels, *i.e.*, bile pigments and acids, and internally toward the lymph and blood channels, *i.e.*, sugar, urea, etc. Since these activities presuppose integrity of the liver cells, it seems logical that functional disturbances such as overloading of healthy cells, or diseases such as infections or toxemias, even without mechanical hindrance to the flow, may change the direction, quantity and quality of these secretions (Quincke). If bile is excreted toward the blood capillaries, and Naunyn considers permeability of the liver cells towards the lymph spaces as the cause of bile parapedesis, icterus must develop (Pick's paracholia, Liebermeister's diffusion-icterus). But doubts have been cast on this theory, especially because very little is known of the forces which can cause bile excretion into the capillaries. Stadelmann, to date, is certain that parapedesis is negligible, so, of course, Naunyn, and others, especially Bauer and Spiegel, support the theory of parapedesis, and even consider it the cause of normal bilirubinemia, since small amounts of this pigment are present in normal blood serum.

Against the theory of parapedesis, are Eppinger's demonstrations of bile thrombi and capillary ruptures (p. 1015). Ogata, on the other hand, believes the bile capillaries merely become permeable during stasis and thus cause icterus without the necessity of rupture. Eppinger's findings have been verified, not only in hemolytic icterus with pleiochromy, for which condition Eppinger claims them as characteristic, but also in mechanical obstructive icterus, (Neukirch, Kretz), and other forms. Indeed, Umber claims that bile thrombi with all their consequences, are the general cause of all forms of icterus. But once more, Minkowski and Sterling, in opposing Eppinger, consider parapedesis the cause of even obstructive jaundice.

Naunyn, by the conception "cholangy" or "capillary cholangitis," means all acute and chronic recurring infectious or non-infectious injuries to the intraacinar bile canaliculi and their contents. He differentiates a secondary cholangy which occurs in obstructive jaundice relatively late, 48 hours after ligation of the common duct, from a primary cholangy of toxic origin, especially that of phosphorus poisoning, in which bile capillaries are blocked by the debris of disintegrated liver cells and cylindrical epithelial exfoliations of the bile ducts (comp. Fischler). The same process occurs in hemolysis. Since he demonstrated an increase of bile acids in the urine in certain cases of infectious icterus, he believes bile stasis is the cause; in others, such as typhoid fever, pneumonia, etc., (see p. 1012), he believes cholangia and parapedesis are at fault.

But doubts have again arisen as to whether all cases of hemolytic icterus can be thus explained (see p. 1012), since hemolytic icterus appears in another form, and the possibility has been revived, especially on the basis of animal experiments, that a direct change of blood pigments into bilirubin may occur extrahepatically or anhepatically to an extent sufficient to lead to general icterus. The reticulo-endothelial apparatus is suspected (see p. 219), especially the spleen and the cells of Kupffer. Minkowski and Naunyn had already demonstrated occasional bilirubin formation by these cells, but lymph nodes and bone marrow also are now under investigation (see McNee's experiments, which, however, are considered quite doubtful by Fischler; see also Ogata, Lepehne, lit.). Hijmans van den Bergh proved that the spleen participated in bilirubin production by demonstrating that splenic blood often contained three times the quantity of bilirubin contained in peripheral blood, whereby, as Naunyn retorts, he proves the extrahepatic origin of bile pigment, but not of "the" bile pigments of hemolytic icterus, and, therefore, does not tell us anything of the nature of icterus. According to Eppinger, the erythrocytes are only "prepared" in the spleen, so that they become easier victims of the bilirubin forming Kupffer cells. It is thought that the liver cells seize part of the bilirubin from the star cells and excrete it in the normal direction of the bile capillaries, in which case bile would enter the blood only in the round-about-way of bile thrombus formation and capillary ruptures (see Lepehne). The other part of the bilirubin remains in the blood by this mechanism as the physiological bilirubinemia. (Hijmans van den Bergh). But if the star cells offer more bilirubin than can be absorbed and excreted by the liver cells, (relative insufficiency), there is overloading of the blood with bilirubin, and an icterus results. Hemolysis is thus an active process, *i.e.*, an expression of the functional capacity of the entire apparatus.

The question of whether these interesting investigations really have proved an extrahepatic icterus is still open. Naunyn considers the elaboration of hemoglobin into bilirubin by Kupffer's cells, which are phagocytic towards almost anything, of no noteworthy importance in bile formation. But hemolysis, the great importance of which he fully realizes, is, according to his opinion, a secondary, and by no means the only cause of hematogenous icterus. Pick cannot believe that histological proof has been adduced of extrahepatic-hematogenous-reticulo-endothelial-lienogenous icterus, and he especially disputes the erythrorhectic process—disintegration of erythrocytes absorbed by cells—that was so extensively demonstrated by Lepehne in Weil's disease. The latter believes that reticulo-endothelial cells are responsible for icterus, but Pick asserts they never could be a cause of it. As evidence of the hepatogenic origin of Weil's disease, Pick points to the cloudy swelling, necrosis and nuclear disintegration of the liver cells and the occasional finding of bile thrombi; he emphasizes the liver necrosis, often visible macroscopically in rabbits, and in addition, that the icterus in splenectomized rabbits inoculated with blood from Weil's disease, is no less severe than that in rabbits which have not been splenectomized, a finding which speaks against the general theory, so frequently put forth, that the spleen has considerable to do with icterus.

To discuss further details would lead us too far astray (see special literature on this matter), (Eppinger, Lepehne, lit., Naunyn, lit.).

Icterus Neonatorum.—As a rule, an icteric skin discoloration appears on the third day after birth with no other symptoms, in about 60% of infants, and disappears in about one week. Severe icterus in the newborn with grave constitutional symptoms, is of septic-toxic origin, or is caused by primary changes in the liver itself, or by pericholangitis gummosa, or by constrictions of the bile ducts (see under syphilis of the liver, p. 940).

Many explanations have been offered for the origin of icterus neonatorum. Since meconium contains no bacteria to reduce bilirubin, Quincke assumed that the non-reduced bilirubin was reabsorbed by the blood directly into the general circulation, because the blood in the mesenteric veins does not flow through the liver during the first few days of life (Elsasser), but passes directly into the vena cava through the open ductus venosus Arrantii. But Knopfelmacher emphasized the physiological improbability of such an absorption process, and assumed there is parapedesis (see p. 1015), or a secretory disturbance because of both the increased viscosity of the bile during the first few days of life and the increase in the amount secreted post partum; the newly formed bile cannot flow off because of obstruction by the old viscid bile in the bile channels. (Compare the older opinion of edema of the bile channels, as a cause of icterus, p. 900.) Miura thinks that swelling of the liver from excessive blood flowing in via hepatic artery and portal vein must impede the outflow of lymph and bile and necessitate an overflow into the capillaries. According to Hofmeier, it is brought about by a sudden and rapid use (destruction) of erythrocytes resulting in an exceptionally abundant and pleiochromic bile with reabsorption of part (hemo-hepatogenous icterus). But this teaching has been both amplified and modified by more recent investigations, which have emphasized first, the disturbed liver function (Heynemann, lit.), and second, the increased bilirubin content of the blood of the newborn (Hijmans von den Bergh, lit.). It has not been verified that bilirubinemia alone means insufficiency of the liver, because numbers of liver cells still functionally undeveloped (post partum), might, like a fetal liver, permit bile pigment to enter the blood, but later, when fully developed, function normally. The hematogenous factor would then be of no importance in this case (Yippo-Hellmuth, lit.). Lepehne's investigations, however, give evidence for the destruction of blood (erythrorrhexis), because he found a breaking down of phagocyted red blood cells within the cells of the reticulo-endothelial apparatus (see p. 1015), especially in splenic pulp cells. The delayed appearance of the direct diazo-reaction (Lepehne) may be of importance in deciding against obstructive causes (see p. 1010), but, on the other hand, this is not easily coordinated with the finding of bile acids in the urine and pericardial exudate (Birch-Hirschfeld, Halberstam). Lepehne is put to explaining this by assuming that they have entered the circulation through an open ductus Arantii after absorption from the bowel. From recent investigations, it seems necessary, therefore, to ascribe a role both to the "hyperactivity" of the blood which takes place in the last days before, and the first days after birth, and to insufficiency of the liver also, which means a hemato-hepatogenous genesis (see Hellmuth, also summary by v.

Taschke). The so-called nuclear icterus, described on p. 1010, is considered by Yippo a phenomenon accompanying icterus neonatorum.

Infectious Jaundice—Weil's Disease.—This is a febrile, septic disease, beginning suddenly with severe general symptoms, such as vomiting, diarrhoea or constipation, weakness, the cerebral symptoms of somnolence and delirium, and muscular pains, especially in the calves of the legs. Icterus is added, and numerous hemorrhages into the skin appear as wheal-like elevations (see Pick). The severity of the disease varies; light ones soon recede; death occurs most frequently in the first and third weeks.

In addition to general icterus, the most striking post mortem pictures are the capillary hemorrhages in serous and mucous membranes, numerous internal organs, especially lungs, and the muscles. They are considered by most observers as infectious-toxic, but Miller thinks they are cholemic (see opposed, Pick, Beitzke a. o.). The heavily jaundiced liver is usually firm, its capsule is smooth, and brown red or wine red points and diffuse spots shine through. The columns of liver cells show slight disassociation, *i.e.*, loosening of the structures, and the pericapillary "lymph spaces" are distended (edema, see Herxheimer). According to most reports, the liver cells are little changed; Pick describes cloudy swelling; many nuclei are swollen and others stain poorly, or not at all. In the central zones is found granular or bile pigment, but bile thrombi may not be present; the liver cells contain little fat although it is often present in considerable quantities in Kupffer's cells; and the formation of giant cells (Oberndorfer). infiltrations of cells, chiefly lymphocytes take place into Glisson's capsule, but this is variable, (see Beitzke), and may be entirely absent. The pathological picture of the liver shows little or nothing characteristic. The large bile ducts are patulous, and the bile is thin.

This jaundice is usually considered a parapedesis bilis, or obstructive from bile thrombi (see Pick). Others consider it the best example of an extrahepatic, reticulo-endothelial-lienogenous jaundice (Lepehne), a view which is vigorously combatted (see p. 1016). Further constant findings are these: in the muscles are macroscopic, small, bile saturated foci of degeneration, microscopically waxy, hyalin, foamy and vacuolar degeneration, hemorrhages and quick formation of granulation tissue (see Pick). The kidneys are markedly swollen, greenish yellow in color, with red spots on the surface; microscopically, there is cloudy swelling to necrosis of the epithelium of some urinary tubules. The capsular epithelium of the glomeruli is desquamated; there are albumen in the capsular spaces and convoluted tubules, small hemorrhages into the tubules and cellular infiltration, chiefly lymphocytic, in the intersititial tissue (Herxheimer-Beitzke). Miller calls this kidney change an "acute interstitial nephritis," with cholemic necrosis, and considers this and the small spotted hyalin degeneration of the musculature of the calves the most important diagnostic findings at the autopsy table.

The spleen is neither swollen nor soft; Lepehne described cells filled with erythrocytes rich in hemoglobin (pulp-cells, reticulum cells—sinus endothelium, see p. 1016).

Contrary to the usual appearance of the liver just described in which necroses play no essential part as they do in acute atrophy, cases have been reported showing the severest injuries to the liver parenchyma with necrosis which points to the possibility of transition of Weil's disease into acute atrophy (Pick, Hart). It may be assumed that a liver showing parts nodular, and parts with ordinary cirrhosis may develop from regeneration in this more or less necrotic organ of Weil's disease.

Etiology.—Weil's disease is also called spirochaetosis ictero-hemorrhagica, because Inado and Ito found in the liver of guinea pigs which had been inoculated with human blood from cases of Weil's disease, a spirochaeta supposedly its cause (see also Uhlenhuth and Fromme, Inada and Kaneko a. o., see their literature). Huebener and Reiter in their experiments with guinea pigs found post mortem conditions analogous to those in man. The spirocheta is designated both as sp. icterogenes (Uhlenhuth and Fromme), and leptospira icterochemorrhagica (Noguchi). It is thought that transmission is via the bite of a louse. According to others, the mucosa of the mouth is the portal of entry. The palate and the pharynx are said to be reddened (Hilgermann), and Miller describes innumerable small vesicles on the epithelium of the tonsillar crypts. The causative organisms are found sparsely scattered in the cadaver in the liver, kidneys, and muscles (see Beitzke); the best hope of success in finding them is in those cases which have died during the first week of the disease and from whom the kidneys are obtained immediately after death (see lit. by Miller, Martin and Petit).

In the atypical form, which closely resembles Weil's disease, but usually shows no icterus,—the so-called seven-day fever,—Nunukayami found a spirochaeta heptomadis, differing from the spirocheta of Weil's disease (see the combined work of Ido, Ito, Wani, Okuda, Hoki; also Kaneko and Morihana).

The autopsy findings in yellow fever closely resemble those of Weil's disease, with the exception of more marked necrosis of the liver cells, especially in the middle zones, while the central and peripheral zones show fatty degeneration (da Rocha-Lima). Noguchi demonstrated an organism in this disease called by him leptospira icteroides. He recovered the organisms in pure cultures and believes they are the causative factor (see W. H. Hoffmann). Transmission is through the mosquito (stegomyia calopus).

PANCREAS

(See Topographical Illustration, p. 140)

Severe diseases of the pancreas are, in general, rather rare.

Malformations

The duct of Wirsung usually empties alongside the common duct into the diverticulum of the (great) papilla (of Vater) situated on the internal edge of the descending limb of the duodenum; as emphasized by Bungner (see, among others, E. Ruge, lit.), before it enters the duodenum it passes for a length of 2 cm. through the pancreatic substance and occasionally alongside the head of the pancreas. But the duct may empty higher (into the stomach), or lower, occasionally into the common duct before its entrance into the duodenal wall. It may even be divided, in rare cases, in the pancreas itself. The plump, short, lateral duct which branches from the duct of Wirsung in the head of the pancreas, opens independently into a smaller papilla in the duodenum and is called the duct of Santorini, (Rozanek found it in 10%). When the main duct is obstructed near its opening by calculi, etc., there need be no retention of secretion because of this accessory duct. According to E. Ruge (lit.), it has little surgical significance, but Clairmont holds a different opinion. See Schirmer, and especially Clairmont (lit.), in reference to variations of the ducts: absence, rudimentary development, closure of the duct of Santorini, or its use as the excretory passage of a small independent accessory pancreas. In fact, the duct of Santorini in communication with the duct of Wirsung may function as a second duct of the pancreas, or may become the chief excretory duct, or even the only one, etc. [See also Mann, F. C., Foster, J. P. and Brimhall, S. D., J. Lab. & Clin. Med., 5: 203: 1920.—*Translator.*]

Accessory glands (accessory or aberrant pancreas) appear as rounded, flattened tumors of the size of lentils to quarter dollars, in the intestinal wall; they may be single or multiple in the duodenum (Thelemann, lit.), upper small intestine (Zenker), stomach (lit. Beutler), rarely in the umbilical region (Wright), indeed anywhere throughout the whole of the small intestine to the valve of Bauhin (Glinski, Serra, lit.), corresponding to the primitive anlage of the pancreas which are developed in the form of numerous small complexes in the wall of the entire small bowel (Broman); they may have independent excretory ducts, sometimes opening on papillary elevations. According to Thorel, they seldom contain islands of Langerhans, (Reitmann, v. Heinrich, lit.) or, if present, they are deformed (Nieuwenhuijse). The author, among others, saw a mushroom-shaped aberrant pancreas the size of a quarter, 4 cm. from the cardia on the lesser curvature in a 41 year old woman with an accessory spleen; it contained islands. Sometimes such an accessory pancreas, which may reach the size of a hazel nut as shown in the collection of Basle, lies at the tip, or even in the mesentery of a Meckel's diverticulum (p. 728). The pancreatic substance is then approximately globular, or coin-shaped, or it fills the apex of the cone-shaped or hemispherical diverticulum; it may also bulge like a ring into the lumen. The glandular tissue sometimes becomes small-cystic. An accessory pancreas itself may lead to the formation of a diverticulum, (Neumann, Glinski, H. Albrecht and Arzt, Albrecht). Duodenal diverticuli are caused frequently by such a structure (p. 749); [or a duodenal ulcer as in the translator's experience.—*Translator*]. Small myomas (adenomyomas) may develop around aberrant pancreatic lobules (p. 806). H. Schmidt described an adenoma of an accessory pancreas of the upper jejunum. See p. 818 in reference to the assumed relation between small intestinal carcinomas and aberrant pancreatic tissue. Division of the pancreas into two equal or unequal parts is rare, as is an annular encircling of the duodenum (Lecco); partial defects are even more rare (Heiberg, Ghon and Roman); absence of the pancreas occurs only in the severest malformations, usually with malformation of the bowel.

Occasionally, small accessory spleens are enclosed in pancreatic tissue. [For aberrant pancreas in the splenic capsule, see Weidman, F., Anat. Rec., 7: 133: 1913.—*Translator*.]

During the agonal period and post mortem, pancreatic secretion may digest the gland itself.

Circulatory Disturbances

In generalized venous congestion, the pancreas is large, vascular, firm, grayish blue. In individuals who die while digestion is progressing, it is large, juicy, soft, cloudy light red (post mortem auto digestion). In anemic and cachectic individuals, it is small, pale and dry. Intravital auto digestion occurs under the influence of circulatory disturbances, especially temporary local ischemia (Blume-Beneke) and arteriosclerosis (Chiari). Hemorrhages into the pancreas and its vicinity are important.

To account for the origin of these hemorrhages, a number of gross and finer vascular changes as well as circulatory disturbances must be considered. According to Seitz, traumatic rupture, *e.g.*, through a fall, is the most common cause (pancreatic and fat necrosis, p. 1041); arteriosclerosis of varying kinds, aneurysms of the pancreatic artery, erosion of the splenic artery by a carcinoma of the pancreas, congestion, decomposition of the blood in sepsis, very marked anemia, etc., are other causes. Hemorrhage is due to diapedesis or rupture, and though unimportant *per se*, is sometimes fatal in its consequences. We must also include degeneration of vessels from fatty changes and lipomatosis of the pancreas (marasmus, general lipomatosis and alcoholism are general causes); the trypsin of the pancreatic juice may erode the blood vessels in hemorrhagic pancreatitis and necrosis (consult chapters III and V). According to Ricker, the diapedesis is neurotic in origin, and according to Marchand, is favored by abnormal reactions of the vessels themselves resulting from injuries such as fat necrosis and autolytic processes in the pancreatic tissue; this explains the quickly produced hemorrhagic infiltrations. According to Knape's theory, purely local irritation of the vascular system may cause hemorrhages and necrosis of the pancreas without any fermentative action, but fat necrosis is always secondary to digestion by the pancreatic secretion. Erosion of vessels due to suppurative inflammation of the pancreas is a possibility. Consult p. 1048 in reference to hemorrhages and cysts of the pancreas.

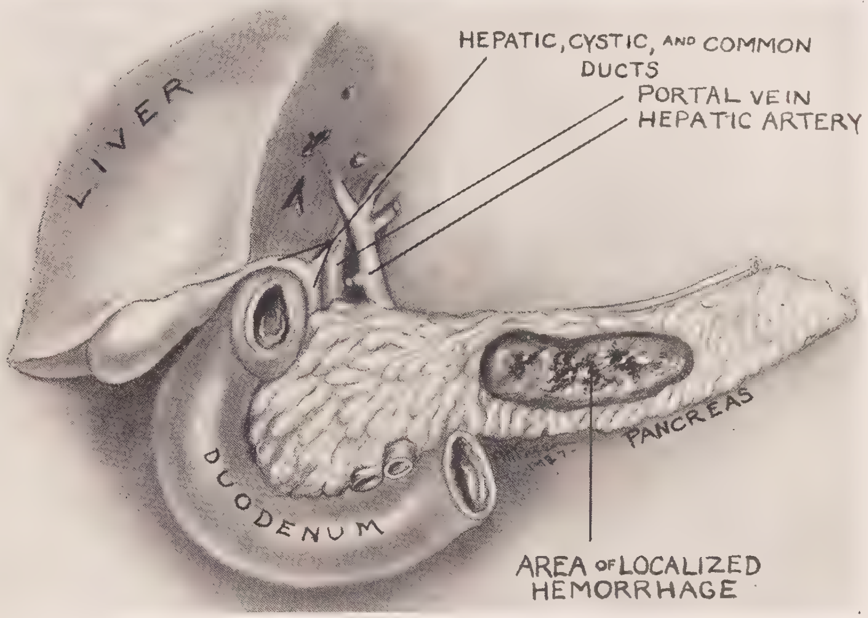

HEPATIC, CYSTIC, AND COMMON DUCTS
PORTAL VEIN
HEPATIC ARTERY
LIVER
PANCREAS
DUODENUM
AREA OF LOCALIZED HEMORRHAGE

FIG. 496.—Localized hemorrhage in the body of the pancreas drawn at operation. Its cause problematic. It destroyed an area of pancreatic tissue as shown in the illustration. There was fat necrosis scattered in the abdomen. L. H.

Hemorrhages vary in their extent. Sometimes they are innumerable but quite minute, and of little consequence, as in advanced anemia. In other cases, a profuse hemorrhage proves fatal, as in erosion of a large vessel by a carcinoma.

The blood is forced directly into the pancreas, the entire structure of which resembles a large blood clot; it spreads toward the spleen, kidneys, liver, omentum, the subperitoneal tissue and the mesocolon. If the wall confining this flow tears, blood reaches the abdominal cavity with resulting paralysis of the heart action and death.

But there occur acute diffuse hemorrhages of the pancreas which are always quickly fatal out of proportion to the magnitude of the hemorrhage or to the exsanguination; for instance, autopsy may reveal perhaps some blood in the duodenum and a blood clot but a few centimeters thick which covers only the pancreas and vicinity. Zenker first reported such observations in which the pancreas showed marked fatty degeneration.

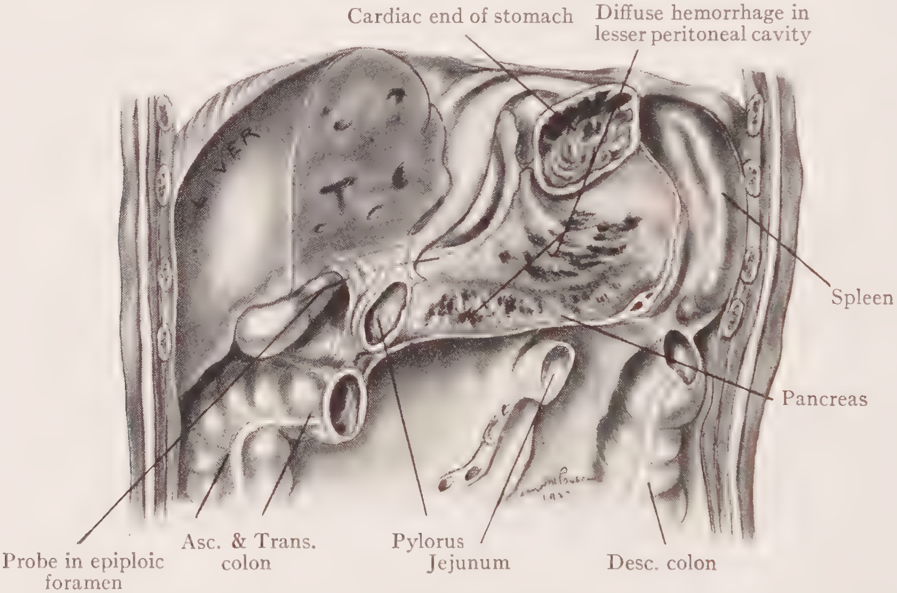


FIG. 497.—Hemorrhage in lesser peritoneal cavity and around the pancreas. So-called pancreatic apoplexy. In this case the pancreas apparently had nothing to do with the hemorrhage for it showed no anatomical changes except saturation with blood on its edges. This condition must not be confused with hemorrhagic pancreatic necrosis from which it can readily be distinguished by the absence of fat necrosis. The cause of the hemorrhage in this case was traced to a sclerotic artery of the pancreatico-duodenal stem. L. H.

How is the death explained? It is thought that the extravasate compresses the large sympathetic nerve complexes, the semilunar ganglion and the solar plexus, with a resultant filling of the abdominal vessels and an empty heart (analogous to the percussion experiments of Glotz), *i.e.*, abdominal shock (Zenker). Seitz emphasizes that this so-called "pancreatic apoplexy" of Zenker influences all reflexes and not merely those of the abdomen, since pressure on the sympathetic ganglia influences the stomach, small intestine, diaphragm, respiration, heart, vessels, brain, (for other explanations, see Kratter, lit.). Frequently this "pancreatic apoplexy" (Zenker) is considered identical with acute pancreatic necrosis

(K. A. Heiberg) and the death, as in necrosis, is due to "pancreatic poisoning" (Lattes, lit.); comp. chapter IV.

Inflammations

Most inflammations are secondary; the primary varieties are rare and obscure etiologically. Secondary inflammations (degenerative parenchymatous pancreatitis) of milder degrees appear during the infectious diseases, such as pyemia, small-pox, and especially typhoid fever. The gland is thickened, opaque, reddened, the cells show cloudy swelling, and the hyperemic interstitial tissue is infiltrated by cellular exudate. If cloudy swelling is followed by fatty degeneration, the color becomes pale, yellowish white, and the consistency softer. In rare cases actual cavities are due to cellular disintegration. Peritonitis may follow. The inflammations may be accompanied by hemorrhage ("hemorrhagic parenchymatous pancreatitis").

Suppurative Pancreatitis.—Purulent inflammations may be due, although rarely, to direct continuity from the neighorhood; *e.g.*, a gastric ulcer may cause a penetrating necrotizing or suppurative pancreatitis, and auto digestion necrosis may be an aftermath (lit. by Kahn and Chiari). Metastatic pyo-pancreatitis occurs in the form of numerous disseminated abscesses in the interstitial tissue. Just as a parotitis may spread from the mouth, so an enteritis may be spread into the pancreatic duct with secondary suppuration of the pancreas (apostematous pancreatitis). The gland swells, becomes hyperemic, firm, spotted, cloudy and peppered with abscesses both in the parenchyma and interstitial tissue; other gland complexes show cloudy swelling, cellular disintegration, or softening, whereas if portions are surrounded by infiltrated interstitial tissue, the nutrition is cut off and they are sequestrated. Even large parts are thus disposed of. This produces a pus or necrotic cavity containing fragments with its wall usually adherent to neighboring organs. Rupture into the bowel or stomach occasionally occurs thus removing the necrotic fragments and actually healing the inflammatory process. A suppurative pancreatitis perhaps originating from surrounding lymph nodes or a gastric ulcer may cause sequestration of the entire gland, (as in the case of Chiari), which is extruded into the bowel as a fetid, discolored mass. A similar rare occurrence was seen by Kahn and Chiari (lit.) in a 55 year old woman with cholelithiasis followed by an auto digestive hemorrhagic pancreatitis, complicated by suppuration due to colon bacilli. Thrombophlebitis may also follow a suppurative pancreatitis with extension into the portal vein (consult the topography, p. 140).

In these severe diseases just mentioned, and even more so in the pancreatic necrosis discussed in the next chapter, cholelithiasis is probably an important etiological factor. See Walter-Sallis (lit.) in reference to non-biliary pancreatitis.

Necrosis of the Pancreas

Acute pancreatic necrosis or hemorrhagic necrosis (Opie and Meakins) or "acute hemorrhagic pancreatitis" is of special interest because of the fat necrosis which at first received more attention than it actually merited.

Clinically, acute pancreatic necrosis occurs in younger men (Korte), beginning with slight pains in the upper abdomen followed by sudden severe pain, vomiting and other symptoms of ileus, distension of the abdomen, facies abdominalis (cyanosis of face), as in perforation of a viscus, ending in fatal collapse (see Zoepffel for lit. as to hematemesis).

At autopsy, part or all of the pancreas is swollen, and inclusive of its surroundings is saturated with blood, and spotted with yellowish white foci of fat necrosis (p. 1038).

The abdominal cavity contains a considerable amount of serous exudate mixed with fibrin from the aseptic irritation of the peritoneum probably due to the foci of fat necrosis (?) (Dreemann). This peritonitis, however, is not the cause of death.

The necrosis is due to the action of activated trypsin on the pancreas, the hemorrhage being due to destruction of blood vessels. The digestion of the fat splitting ferment, steapsin, is only of incidental importance. (Consult animal experiments of Rosenbach, O. Hildebrand, Dettmer, Guleke, Hlava and others cited in chapter on necrosis of fat tissue, p. 1039.)

How does the pancreatic juice develop this auto digestive property, and under what conditions does it become active? Normal pancreatic juice, strongly alkaline, secreted into the intestine, contains three ferments, but they require the presence of a foreign activator, enterokinase, to render them active: (*a*) pancreatic diastase or amylase changes starch into sugar; (*b*) trypsinogen is the prestage of trypsin which changes proteins to peptone; (*c*) lipase or steapsin splits neutral fats. Further constituents are: albumen, xanthin, leucin, guanin; and among inorganic factors: calcium carbonate, calcium phosphate, alkaline earths. In addition to its external secretion, the pancreas also produces an internal secretion, which, among other purposes, has a regulating influence on carbohydrate metabolism especially on the oxidation of sugar. Boldyreff showed that the introduction of fat into the stomach causes antiperistaltic movements of the duodenum to expel its contents through the pylorus into the stomach. Vomitus, and the stomach contents removed by tube, are often bile stained from reflux of duodenal contents. According to Gross, the rule is for duodenal contents to flow backward into the stomach and produce a diastatic action from the diastase derived from the pancreatic juice.

Since, therefore, the pancreas itself contains inactive proferments which require a foreign activator, and since this latter is physiologically a kinase (enterokinase, Pawlow), it follows that ascending bile is of great importance in activating the juice within the gland itself. As emphasized by Opie, Fuchs, Simmonds, and many others (v. Haberer, and consult p. 1042), pancreatic necrosis is frequently related to cholecystitis, because, according to Opie, bile stasis permits the ascent of bacteria-containing bile (chiefly colon bacilli) into the pancreas. It is known that bacteria can activate the pancreatic juice (Polya), but bile alone can also accomplish this act, as well as ascending duodenal contents (Nordmann); indeed, blood is also an activator, for observations show that spontaneous and traumatic hemorrhages into the pancreas produce the picture of pancreatic necrosis (Borchardt, lit.). Thus it is clear that pancreatic necrosis is merely a symptom of different processes which create conditions suitable to the passage of the digestive juice into the pancreatic tissue (see Bode).

Opinions are in conflict in reference to the mechanism of the hemorrhages (p. 1022), but the statement that they are secondary to vessel erosion due to the digesting pancreatic juice, receives the greatest support. Hlava, on the basis of experimental injections of hydrochloric acid, supposes that hyperacid gastric juice enters the pancreas causing thrombosis and subsequent hemorrhages and necrosis; Ricker assumes that stagnant pancreatic juice causes stasis and capillary hemorrhages through vasomotor irritation, and that since activation of the ferments is not necessary, stasis is followed by necrosis.

What is the cause of death in pancreatic necrosis? It has been mentioned that it is not peritonitis (p. 1026). Death is really due to general intoxication. As active poisons, soaps have been mentioned (Hess), or the secretion of activated trypsinogen (v. Bergmann and Guleke) or the products of autodigestion of tissue (Doberauer, Babitzki, lit., lit. by Guleke, Lattes). Others believe death results from shock (p. 1024).

The fate of pancreatic changes in subacute and chronic pancreatic necrosis. Formation of pseudocysts. If death is not prompt, the process may become localized with the formation of an irregular ragged cavity. Progressive disintegration and softening by the action of trypsin and hemorrhages due to erosions of vessels, produce a mushy material filling the cavity which occupies the pancreas or reaches backward and downward far beyond its borders (into the omental bursa); at times, the only parts recognizable are necrotic, opaque, yellowish brown, smeary remnants in the anterior wall of the pseudocyst. Foci of fat necrosis are present in large numbers. Not rarely, secondary infection from the bowel is added, and pus fills the cavity so that it may be called "hemorrhagic pancreatitis." The older the cavity, the better the encapsulation by granulation tissue, and the better developed the cyst, adherent to its surroundings; it then contains a cloudy, thick, grayish yellow, or by blood admixture, brown, fatty, sometimes coarsely grumous poultaceous mass, looking like bloody pus, but containing no cells or nuclei. The author saw such a case quite remarkable on account of the advanced age of the individual (84 years). A similar case in advanced age has been found only by Hlava. In a 36 year old woman, the cicatricial cystic sac contained 2 liters of a gray green thin fluid mixed with discrete grayish green black clumps; it lay behind the stomach and transverse colon and reached posteriorly almost down to the promontory, to the left to the spleen, which was completely enveloped in fibrous adhesions. In comparatively early sacs, masses and fragments of the gland may be recognized, rarely larger pieces, or perhaps only trabeculae-like floating tissue fragments; in old sacs nothing can be identified. Rossle saw white globules of sebaceous material. The sac enlarges as long as the digestive action of the pancreatic juice persists or suppuration continues, or hemorrhages occur, but in a few months, it undergoes cicatricial changes. Finally, it becomes stationary. Durings its development, however, a fibrino-purulent peritonitis or deep abscess formation or erosion of neighboring arteries can occur. Thus Reinhardt saw perforation into the sac of an aneurysm of the superior pancreatico-duodenal artery.

The differential diagnosis between similar cavities, and sacs due to suppurative pancreatitis is quite difficult.

Remarks in reference to the designations "acute pancreatic necrosis" and "acute hemorrhagic pancreatitis."

Inflammation, as indicated by the name "pancreatitis (acute hemorrhagic)," is not essential in pancreatic necrosis. But a complicating infection, usually by colon bacilli, may be added; there is no doubt that inflammation of the large bile ducts in cholelithiasis may allow bacteria to ascend the congested duct of Wirsung. If the process in the pancreas is essentially bacterial, there results a suppurative pancreatitis; but activation of the pancreatic juice with subsequent pancreatic necrosis can be accomplished by bile, whether it contains bacteria or not. Thus, there are a purely chemical, aseptic acute pancreatic necrosis, and one due, or connected with, infectious inflammation, formerly called "acute hemorrhagic pancreatitis" because the inflammation was unduly emphasized, whereas the necrosis is the essential thing.

Fibrous Chronic Interstitial Pancreatitis.—This is focal, when a peptic ulcer impinges on the pancreas (fig. 300, p. 686). In diffuse fibrous pancreatitis there is proliferation of the inter- and intra-acinar tissue with destruction of the glandular tissue. The gland as a whole may be enlarged or diminished in size, as thick as a finger, or quite flat, exceedingly hard, light gray in color, grating on section, while the acinar design may be completely lost. The pancreatic duct is usually enlarged. The condition is called pancreatic induration, pancreatic cirrhosis, atrophic cirrhosis, etc. Sometimes the change is especially marked in the head of the organ, which becomes hard and thick in the so-called "tumor-like chronic pancreatitis" which clinically may be mistaken for carcinoma. Compression icterus is possible (comp. v. Mosetig). The induration is secondary to chronic

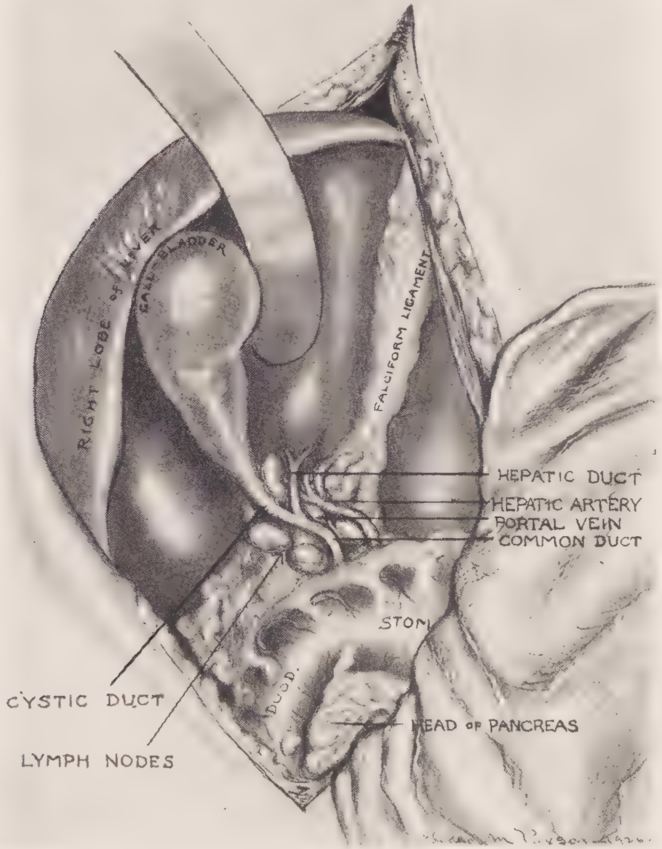

RIGHT LOBE of LIVER
GALL BLADDER
FALCIFORM LIGAMENT
HEPATIC DUCT
HEPATIC ARTERY
PORTAL VEIN
COMMON DUCT
STOM
DUOD.
HEAD of PANCREAS
CYSTIC DUCT
LYMPH NODES

FIG. 498.—Cholecystitis with lymphangitis, lymphadenitis and sclerosis of the head of the pancreas. Sketch made at operation. This is the train of events made famous by the surgeon. Infection in the gall bladder, lymphangitis, lymphadenitis, first of the node at the junction of the hepatic and cystic ducts, then of the nodes along the common duct, then lymphangitis around the head of the pancreas with extension into the pancreas itself and subsequent sclerosis. See text for discussion of another theory of the mode of origin of cirrhosis of the head of the pancreas. ½ nat. size.

catarrh, calculus formation in the duct of Wirsung, gall stones in the common duct (Fuchs, Opie), carcinoma of the head or body of the pancreas or of the common duct (fig. 505); or is primary, especially in congenital syphilis, more rarely in the acquired. The first forms produce diffuse fibrosis, the second forms circumscribed white scars. The pancreas is harder than normal; in cirrhosis of the liver it must be remembered, however, that the pancreas is normally fairly firm, but not as firm as in the moderate degrees of diffuse interstitial pancreatitis as found in hepatic cirrhosis (consult Steinhaus, D'Amato, Lando, Poggenpohl, lit.). The islands (p. 1035) are usually unchanged, but occasionally show sclerosis and atrophy (diabetes may appear). Alcohol has been considered an etiological factor (Friedreich, Lissauer); according to Simmonds, it causes

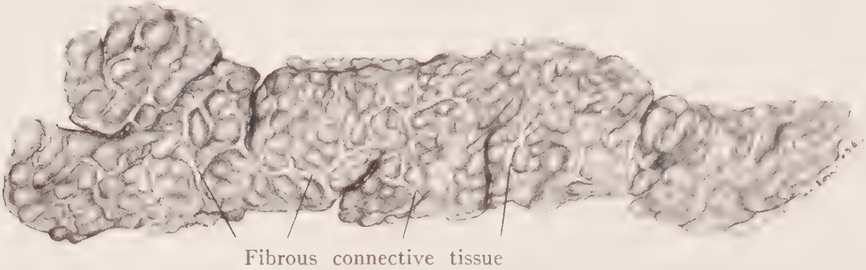

Fibrous connective tissue

FIG. 499.—Chronic interstitial perilobular pancreatitis throughout the organ. Such an organ is hard, tough, shrunken and small and shows decided lobulation, each lobule appearing almost as a nodule jutting far out beyond the level of the connective tissue stroma which separates it from its neighbor. L. H. ½ nat. size.

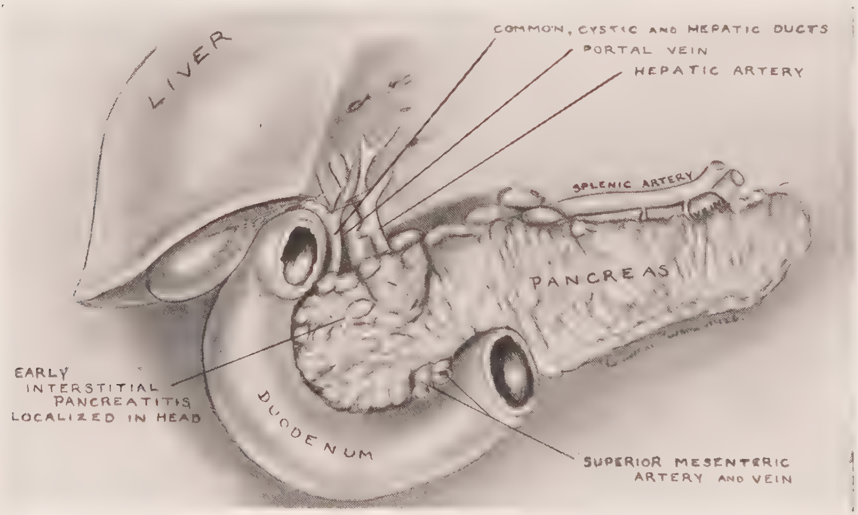

LIVER
COMMON, CYSTIC AND HEPATIC DUCTS
PORTAL VEIN
HEPATIC ARTERY
SPLENIC ARTERY
PANCREAS
EARLY INTERSTITIAL PANCREATITIS LOCALIZED IN HEAD
DUODENUM
SUPERIOR MESENTERIC ARTERY AND VEIN

FIG. 500.—Early interstitial pancreatitis localized to the head of the pancreas. The remainder of the pancreas is of normal consistency. This type has led to much discussion among surgeons as to the etiology. See text. L. H. ½ nat. size.

diabetes by injuring the pancreas; indeed, in such cases, it may lead to marked hemochromatosis (bronze diabetes, p. 926). Symmers found large collections of fat in the islands of Langerhans in some chronic alcoholics. See p. 926 for pigment cirrhosis in diabetes.

Translator's Remarks.—The fibrosis which appears almost exclusively in the head of the organ and not in the body has assumed some surgical importance from the standpoint of etiology. It is found quite frequently in connection with long standing infection of the gall bladder. According to the lymphatic theory, infection drains downward from the gall bladder, producing first a pancreatic lymphangitis and finally pancreatitis in the head of the organ. According to the duct theory, the infection ascends the duct of Santorini from the common duct. The importance of the lesion is judged differently by different observers; most sur-

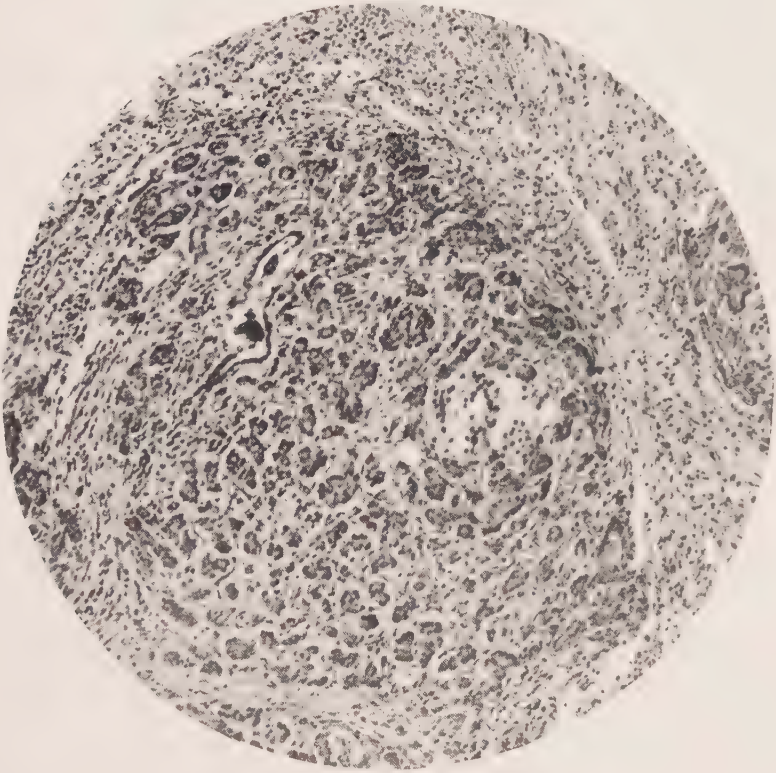


FIG. 501.—Chronic intra- and interlobular interstitial pancreatitis. The connective tissue divides the lobules of the pancreas into isolated units, encroaching upon them from the periphery which reduces their size. Small strands entering the lobules also separate the individual acini. An island of Langerhans in the illustration shows that no connective tissue is present within it. The apparent disintegration is quite probably a post mortem change. × 120. L. H. #148.

geons believe it is a serious sequel of neglected gall bladder pathology. It is recognized grossly by the hardness localized in the head and microscopically by the connective tissue increase. The translator discovered one case at autopsy in which the arrangement of ducts was such as to preclude the possibility of duct borne infection; therefore the lymphatic route is at least possible. But see Deaver, J. B., Pancreatic Lymphangitis, Surg., Gyn. & Obst., 28: 433; 1919, and Deaver, J. B. and Sweet, J. E., Prepancreatic and Peripancreatic Disease, J. A. M. A., 77: 194, 1921. For duct borne infection see Kaufmann, M., Surg., Gyn. & Obst., 44: 15, 1927.

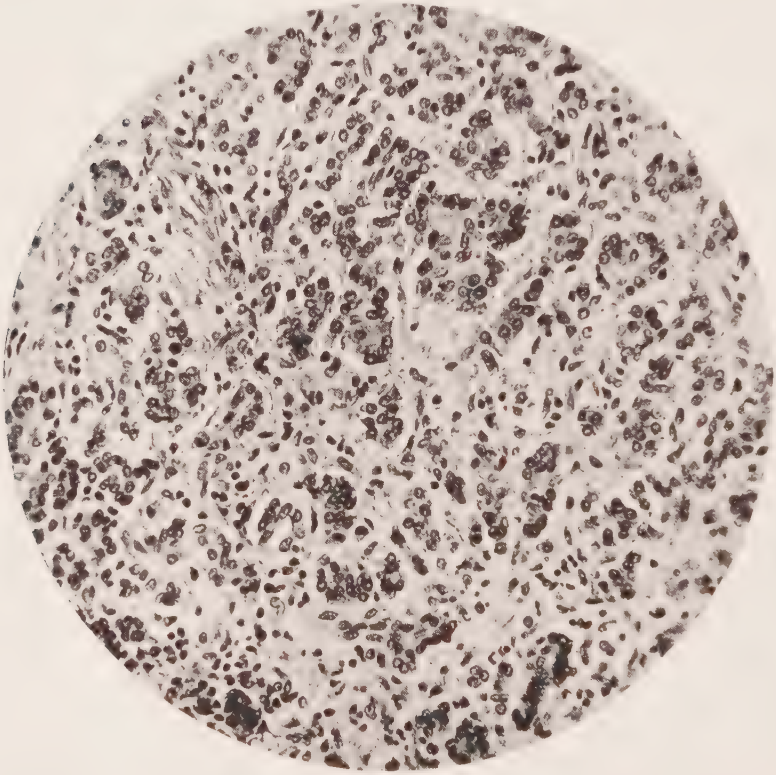


FIG. 502.—Chronic intralobular interstitial pancreatitis. The increase in connective tissue extends to within the lobules where it separates the acini into individuals and small groups. It sometimes invades the islands of Langerhans but as a rule leaves them free. It is probably a factor in their destruction at times. × 300. L. H. #148.

Infectious Granulation Tumors

Syphilis (fig. 205, p. 464).—In the diffuse interstitial fibrous pancreatitis of congenital lues, the organ is more or less enlarged, thick and hard, and on section smooth, bacony, granular, and cloudy grayish white.

Great numbers of spirochetae cause marked development of connective tissue around and within the lobules and around the ducts, but the changes vary in degree. This inhibits the development of the parenchyma (see Kimla, Stoerk, and others). If the formation of new mesodermal tissue begins in early fetal life, the development of the islands is hindered, although not checked, because they are relatively numerous and well preserved (Mills Pearce), but, nevertheless, still attached to the branches of the ducts. Furthermore, the development of islands into acini (Marchand and others) is impeded; in severe cases the latter are few in number; the absolute number of islands is also diminished (Seyfarth, lit.). Gummas are very rare, but do occur up to the size of almonds even in the newborn; in acquired syphilis they occur from microscopic size to the size of a child's fist; pancreatic cirrhosis is also present (diabetes may be absent) (Schlagenhaufer, Thorel, Koch, Seyfarth). Occasionally, the gummas contain numerous giant cells of the Langhan's type. Tuberculosis of the pancreas is rather rare; miliary tubercles in the interstitial tissue, and larger tuberculous foci, extending from adjacent lymph nodes have been observed; diabetes may be present (lit, by Seyfarth). Kirch (lit.) speaks of tuberculous cirrhosis of the pancreas as the result of a granulating tuberculous inflammation.

Atrophy, Degeneration, Fat Necrosis of the Pancreas

Atrophy of the pancreas with small lobules and considerable loss of weight to 40 gms. or less, (90 to 120 gms.; according to Vierordt, 97 gms., is normal), is fairly frequent in senile and pathologic marasmus, also in diabetes, usually of younger individuals. The findings are far from constant (for functional hypertrophy of the pancreas, see Rossle).

In some cases of severe diabetes mellitus (with polydypsia, polyphagia, polyuria and mellituria), lipomatosis of the pancreas is found; in others cirrhotic atrophy, in relatively rare cases, brown pigmentation (diabete bronze, see p. 926). In other cases of pancreatitis, however, there is no diabetes, and in young diabetics, visible pancreatic changes are frequently absent (comp. Holasz); indeed, the pancreas may be macroscopically intact (Weichselbaum). This does not exclude qualitative or quantitative changes in the islands (see p. 1036). E. J. Kraus believes the eosinophilic cells of the anterior lobe of the hypophysis are regulators of sugar metabolism. Among other things, marked decrease in the number of these cells, especially in younger diabetics, is supposed to be an expression of impairment of the regulatory function of these cells which suffer, because they try to lift the burden from the insufficient apparatus of the islands. Verron could not verify these findings. In reference to diabetes on hypophyseal grounds, see Brugsch. In dogs, complete extirpation of the pancreas causes diabetes mellitus (v. Mering, Minkowski and others). This led to the deduction that the integrity of the pancreas (*i.e.*, its internal secretion) is of importance in the normal sugar consumption of the body (comp. E. Pfluger, Blumenthal). See Bode as to diabetes after operations or accidents. The lack of resistance of diabetics to suppuration is of practical importance. Consult Ribbert for hereditary diabetes and its anatomical basis, and P. F. Richter on the present viewpoint in diabetes.

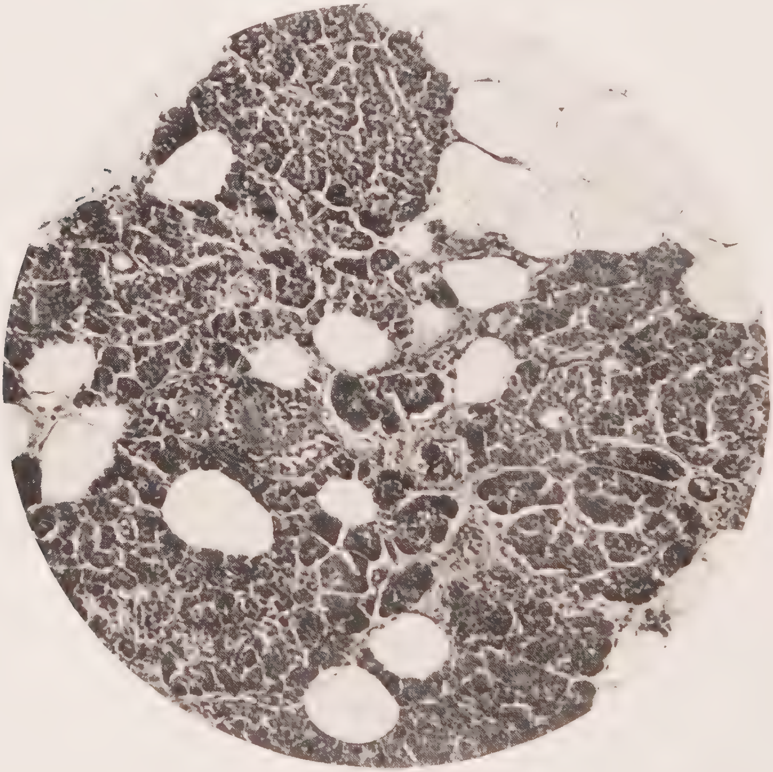


Fig. 503.—Fat infiltration of the pancreas. This patient was not generally adipose and had no diabetes. Since, however, diabetes is apparently a function of the number of islands left in a pancreas, such lesions as fat infiltration, by destroying portions of the pancreas, may well destroy enough to produce varying degrees of diabetes. × 120. L. H. #136.

In 40 cases of pancreatic diabetes, v. Hansemann described atrophy in 36, characterized by flabby consistency, darker color, flatness and firm adhesion to the surrounding connective and fatty tissue (in contradistinction to the sharply demarkated cachectic atrophy). This author suggests an interstitial inflammatory process, or granular atrophy, called by Opie intra-acinar sclerosis, in which the connective tissue is increased and infiltrated with small cells. In the granular atrophy, v. Hansemann assumes that the gland structure as a whole is preserved, but Reitmann, in this change, called by him "diabetic pancreatic cirrhosis," demonstrated extensive alterations in the entire gland architecture due to degeneration. Herxheimer considers diabetic cirrhosis of the pancreas a change brought about both by degenerative processes with marked development of connective tissue, and by regenerative processes, especially of the islands. This corresponds in a way to cirrhosis of the liver (Kretz, see p. 924) with the difference that the progressive connective tissue proliferation is much more marked in the liver.

Especial attention has been directed to the character of the islands in diabetes and their reduction in number and size. Various changes have been described, such as simple atrophy, sclerosis, hyalin, hydropic degeneration, round cell infiltration, hemorrhages, vascular changes—the latter of which, according to v. Halasz, are confined to the islands or involve the whole gland—as well as regeneration and hypertrophy; this latter, according to Cecil, occurs in two types, (*a*) simple hypertrophy, and (*b*) regenerative hypertrophy—complexes of anastomosing columns of cylindrical cells. But the statements as to the frequency of these changes and the conceptions as to their relation to diabetes are so contradictory that reserve is advisable; indeed, the histogenesis, anatomy and physiology of the islands are still subject to much dispute (lit. in appendix).

The irregular, mulberry-shaped epithelial "intertubular cell masses" or islands of Langerhans, consist of branches, nets and strands of epithelial cells between which are capillaries; according to Opie, v. Hansemann, and others, there are twice as many in the tail as in the rest of the gland (comp. K. A. Heiberg); according to some, they are surrounded by a fibrillar capsule (Marshall Flint Weichselbaum), but all authors do not agree on this point (Herxheimer and others). They have no connection with the external secretion, but are endocrine organs or glands (p. 496) functioning in the regulation of the carbohydrate metabolism and the sugar content of the blood (W. Schultze, McCallum, Kirkbride and others). According to later investigations, the islands are neither anatomically nor physiologically independent of the rest of the gland; the internal secretion with its disturbance in diabetes is related both to the islands and acini, so that the centro-acinar cells have an internal secretory capacity similar to that of the islands (Seyfarth, lit.).

While Karakascheff, and others (see note p. 1049) consider the islands as replacement organs from which gland parenchyma may be produced, Herxheimer, conversely, assumes the islands regenerate from acinar tissue (and resting islands), a statement supported by Marchand who otherwise accepts the viewpoint of Karascheff (see McCallum, Gelle, K. Koch, etc.). On the other hand, this exchange between islands and gland tissue (tubules) is doubted by Helly, K. A. Heiberg, etc., who consider the islands specific organs. Weichselbaum believes that new islands may come from the ducts (see Gontier de la Roche) and also, as investigations of Kyrle (on animals) have shown, that islands may regenerate from others; he nevertheless considers it doubtful, as does Kyrle, that they can come from acini (Seobolew). Gelle (lit.), however, supports the idea of metamorphosis of islands into acini (acino-insular form) and of acini into islands (insulo-acinar form; see Laguesse), and proved it in vertebrates (good illustrations). Seyfarth testifies to the continuous new formation of islands from small ducts throughout life, according to necessity; he does not consider the islands specific organs, but only special developmental forms of the secreting parenchyma, foci, as he calls them, from which the principal part of the parenchyma originates in fetal and post fetal life. They are thus a prestage in the development and in the regeneration of the parenchyma. It can be stated: in certain diseases such as diabetes, but especially in old age and in inanition, functioning parenchyma does not involute backward to islands.

The so-called "island theory" which assigns an essential, indeed an exclusive, influence in diabetes to changes in the islands is based on the anatomical investigations of Dieckhoff, Scobelew, Opie, Weichselbaum-Stangl, Massaglia, etc. Sauerbeck (lit.) found the exclusive or predominant lesion in the islands in diabetes; without diabetes, island lesions are rare, while with diabetes they are only exceptionally absent. Others deny the exclusive importance of alterations of the islands in diabetes (v. Hansemann, Karakascheff, Reitmann, Herxheimer, Gelle, Fahr, Seyfarth and others) and consider disease of the whole gland inclusive of the islands, as the chief factor, while perhaps but a small fraction of the islands are diseased and never they alone. But in addition to qualitative changes, K. A. Heiberg (lit. up to 1910) with his counting method, always found a marked decrease in the number of islands (instead of 130 islands per 50 ccm. of gland, there were but 30 to 40). He therefore considers these quantitative changes as decisive in diabetes, especially in such cases which formerly eluded our methods of investigation. Weichselbaum (lit.), after extensive study, emphasizes forcibly the constancy and dominating importance of changes in the islands, especially the qualitative changes. On the basis of 183 cases of diabetes, he differentiates 3 forms distinguished by various conditions of the islands and gland tissue: (1) hydropic degeneration followed by atrophy; the islands are small and tiny, cells resemble lymphocytes. Very frequently, a most irregular atrophy of varying severity is found in the parenchyma. K. A. Heiberg, a staunch supporter of the "exclusive island theory," considers it possible that this atrophy without connective tissue increase may be related to the loss of water in coma. This is the most frequent form and is often found in severe cases. Early life is preferred; cause unknown—(hereditary factors, congenital weakness); regenerated islands may also undergo hydropic degeneration. (2) Chronic interstitial pancreatitis causes connective tissue proliferation in the islands with sclerosis and atrophy. There are often marked proliferation of fatty tissue, a lipomatosis of the pancreas, and also arteriosclerosis of the pancreatic arteries. The gland parenchyma is atrophic, corresponding to the degree of proliferation of the connective and fatty tissues. This form, in which the course is chronic, favors advanced age. It is also seen in pancreatic lithiasis. Regeneration and hypertrophy occur of both islands and gland tissue. (3) Hyalin degeneration of the islands, rarely pure, usually combined with (2) is perhaps merely a subtype of it, but the course is more severe, it chooses more advanced age, and arteriosclerosis is very frequent; Herxheimer identified hyalin degeneration of the islands with arteriosclerosis (see v. Halasz), while Weichselbaum believes they are two different processes. But arteriosclerosis is probably of causative importance (G. Hoppe-Seyler) in the primary interstitial change in the pancreas, as are foods, alcoholism, syphilis and tuberculosis (Seyfarth, lit.) and not rarely a familial hereditary element, (consult Herxheimer). After consideration of the literature (see there), and personal investigations, Seyfarth discarded the "island theory." Injury to the parenchyma and the islands leads to diabetes; the islands are the more important factor, but not the only one. Herxheimer expressed himself in quite similar terms shortly before. The burden of proof now seems to rest on the supporters of the exclusive "island theory."

The feces are extraordinarily rich in fat in advanced atrophy when the gland is transformed into a flat, almost translucent and almost purely fibrous strip (fibrous atrophy) in which the thin dilated duct is recognizable.

Translator's Remarks.—For further data on the pancreas and diabetes, see Allen, F. M., Glycosuria and Diabetes, Boston, 1913, and with Stillman, E. and Fitz, R., Rock. Inst. Monograph No. 11. For discussion of the pathological anatomy, methods of staining, critique, etc., see Bensley, Harvey Lectures, 1915; Major, R. H., J. Med. Res. 31: 313: 1914 and 1915. For insulin, see Macleod, J. J. R., Physiol. Rev. 4: 21: 1924. A most interesting case from the pathological physiological viewpoint is presented by Wilder, Allan, Power and Robertson (J. A. M. A. 89: 348, 1927). A patient presenting spontaneous hypoglycemia required hourly doses of glucose to prevent the convulsions. The blood sugar fell below 0.03% when this was delayed. At autopsy there was revealed a carcinoma probably originating in the islands of Langerhans with metastases to the liver and lymph nodes. Alcoholic extracts made from the carcinoma tissue acted like insulin on injection into rabbits. In a case observed by the translator and reported by Hartmann, F. W. at the Philadelphia Physiological Society in 1923, the patient stated that if he did not eat every two hours he "threw a fit." This was found to be a hypoglycemic convulsion, the blood sugar falling to 0.03% and lower. Various procedures were tried such as the giving of adrenalin and pilocarpine without results. On the basis of the patient's history and a plus four blood Wassermann reaction, the patient was given vigorous antisyphilitic treatment, whereupon his symptoms disappeared so that he was able to withstand a fast of about six hours. He nevertheless carried a number of lumps of sugar and every hour or two would eat several. Nothing, of course, is known of the pathological anatomy of the individual.

Amyloid degeneration may be part of a wide spread amyloidosis of the organs. It occurs chiefly in the vessel walls, but partly in the connective tissue around the glands. The parenchymatous cells may undergo some fatty degeneration, or simply die from atrophy (see Butterfield).

Simple fatty degeneration of the gland cells occurs in phosphorous poisoning. Opinions are divided as to fatty degeneration in diabetes (v. Hansemann, Karakscheff, Weichselbaum).

Brown pigmentation of the epithelium occurs in senile atrophy and to greater degrees in general hemochromatosis (see p. 928), especially in drinkers. Pigmentation in diabeté bronze is discussed on p. 927; in this disease, pigment lies in the interstitial tissue also.

In lipomatosis, the fibrous interstitial tissue is transformed into fatty tissue; in more advanced degrees, the gland cells are infiltrated and partly crushed by fat; in the highest degrees, the whole organ becomes a thick, long, slightly nodular mass of fat, so that macroscopically, only the pancreatic duct with its larger branches, and isolated cloudy gray spots, remain of the former gland. The weight may be increased (see Rossle); the islands may remain well preserved (p. 1035). There does occur, however, a lipomatosis of the pancreas with changes in the islands and diabetes (p. 1035, consult Weichselbaum). In one-half of these cases, a chronic interstitial pancreatitis is also present.

Fat necrosis (Balser), more correctly, necrosis of fatty tissue of the pancreas, (fig. 505), is a condition formerly much overrated in its pathological importance; it consists essentially of the escape of the pancreatic enzyme steapsin from the gland lobules, and the exertion of its powers to kill fatty tissue. Leakage occurs in very many conditions. Even though the fat necrosis itself is of pathological importance in only rare cases, it nevertheless is a striking and important picture (especially surgically) since it indicates some severe change in the pancreas. It is always present in pancreatic necrosis (p. 1026), and for this reason is found, like the latter, in obesity (men, drinkers) and in cholecystitis (see Moser, who attempts to explain the selection of adipose individuals).

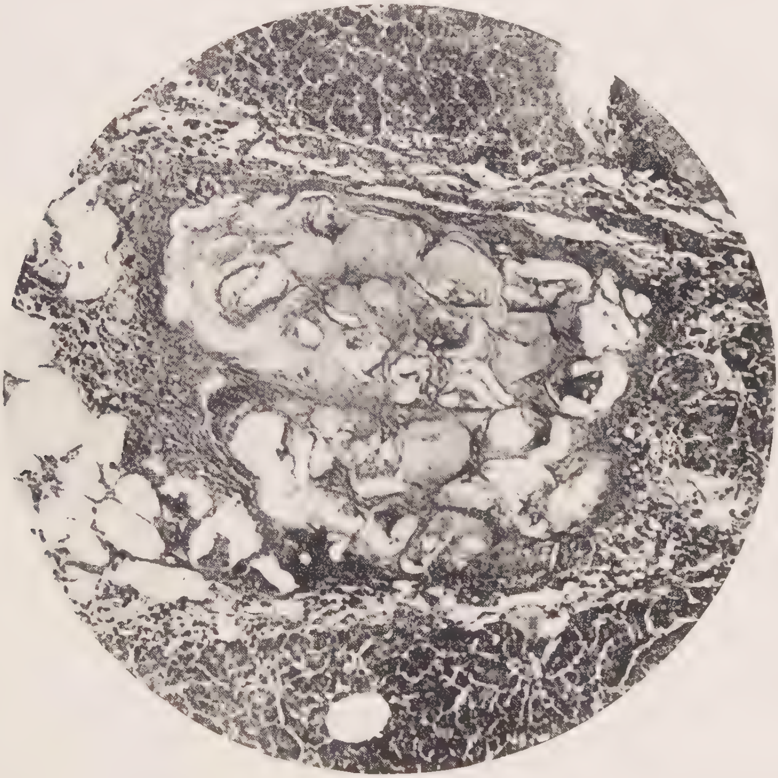


Fig. 504.—Fat necrosis in the pancreas. The remainder of the pancreas in the section shows relatively minor changes, the escape of pancreatic juice having probably occurred from the neighborhood of the head of the pancreas where most of the trouble was localized. × 120. L. H. #145.

It occurs chiefly in the fatty tissue of the pancreas and its vicinity, but also in that of the omentum, mesentery or in the subperitoneal and even subpleural, subpericardial and subcutaneous tissues. Small areas of fatty tissue undergo necrosis; sometimes the areas are of the size of pin heads or smaller, rarely larger than lentils (size of a finger nail). They are opaque, white, yellow white or gray white in color, in icterus yellow or deep green, soft, almost liquid or harder, easily crushed, like stearin.

Occasionally, they are surrounded by a reactive red halo. Those of harder consistency can often be lifted out with the point of a knife.

The foci of fat necrosis may enlarge and increase in numbers post mortem (Thorel). With Benda's reagent (cupric sulphate solution, tissue hardened in formalin) the foci become green, as with Weigert's copper-chrome-alum-acetic acid mordant.

Microscopic examinations of stained sections show no nuclei in the foci. The network of fatty tissue is filled with granular radiating fatty acids staining red with hematoxylin and eosin. But if the fatty acids remaining after absorption of fluid combine with lime (R. Langerhans) the color reaction is blue. Fatty acid-lime is insoluble in hydrochloric acid, soluble in glacial acetic acid and pure sulphuric acid (after long exposure) with the formation of gypsum crystals. As Reitmann has shown, a secondary zone of fat necrosis appears around the first focus, because wandering cells which arrive in some numbers are also killed. Then a typical reactive inflammation develops, leading to more or less extensive absorption, or to the formation of an encapsulating connective tissue envelope; since this envelope encloses liquefying contents, small cysts are frequent. Enlargement to disintegration cavities is due to a combined action of steapsin and trypsin, *i.e.*, an auto-digestive effect of activated pancreatic juice (cf. Chiari, Pforringer and others). Foci of true pancreatic necrosis must be considered in the same light, when found, as happens occasionally, between the closely grouped foci of fat necrosis; the lobules undergo necrosis, and the cells become pale, vacuolated masses with unstained nuclei fusing into granular aggregates.

Absorptive processes dry the areas so that crystalline deposits occur, while phagocytes take up droplets and debris (steatoclasts of Reitmann, thought by Basler, but erroneously so, to be proliferating fat cells); other cells such as giant cells, eosinophiles and fibroblasts are abundant, and the foci are encapsulated by fibrillar connective tissue (Reitmann). In this way healing is completed.

The essential factor in the development of fat necrosis is the fat splitting ferment of the pancreatic juice; steapsin splits neutral fats into glycerin and free fatty acids (a process corresponding to fat turning rancid); after the liquid components are removed, the solid fatty acids remain, and may combine with lime as in the formation of adipocere, fat-wax, etc., (lit. Ascarelli, Mita, Burger, Furth, M. Muller). Flexner demonstrated the presence of the enzyme in the foci. The opinions first expressed by Langerhans are supported not only by numerous animal experiments (Langerhans and especially O. Hildebrand, also Korte, Oser, Opie, Flexner, Fr. Rosenbach, etc.) but also by observation on humans (lit. to 1901 by Truhart, to 1912 by Albrecht, and lit. in appendix). Payr and Martina in experimental investigations, point out that a small amount of necrosis of fatty tissue is due to embolism of pancreatic cells released by crushing. But embolism of pancreatic cells occurs in the liver also, as well as fat infiltration and fat splitting (Brenner) so that necroses in the liver (Oestreich, Adamski) and in the adrenals (Kaiserling) are produced occasionally by these emboli.

According to Eppinger jr., stasis alone is insufficient to cause necrosis of fatty tissue; it needs activation of the pancreatic juice by duodenal contents, bile, bacteria, etc., (for details, p. 1026). Numerous foci of fat necrosis in the peritoneal cavity are probably not due to the entrance of pancreatic juice directly into the peritoneal cavity, because they are covered by well formed cells, but are caused in part by entrance and diffusion in retro- and subperitoneal tissues, and in part, according to Eppinger, by pancreatic cells or even whole fragments of acini containing active secretion carried in blood and lymph vessels (comp. necrosis of liver). (See experiments of Erugoni and Stradiotti, Fr. Rosenbach.) According to most evidence, steapsin is easier to activate than trypsin; necrosis of fatty tissue is frequently seen without coincident autodigestion by trypsin. Pancreatic juice may escape, *e.g.*, from traumatic rupture of the pancreas, and cause only fat necrosis, often over large areas without other pathological changes in the pancreas. Naturally, there are cases in which

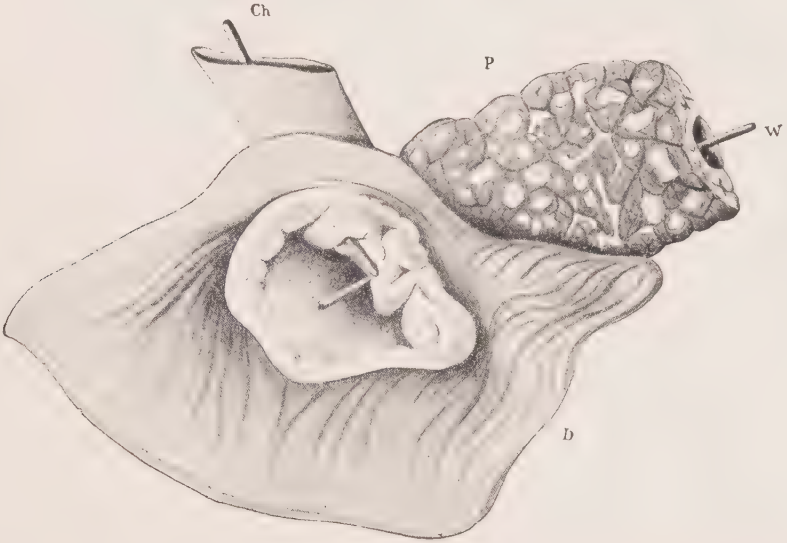


FIG. 505.—Fat necrosis of pancreas (P) due to a narrow duct of Wirsung caused by an adenocarcinoma of the duodenal papilla; foci bile stained. Narrowing of the common bile duct, its inner circumference invaded by the carcinoma; behind this, marked dilatation of the common duct (Ch), and the duct of Wirsung (W); D, duodenum. Behind the indurated head of the pancreas (but without carcinomatous infiltration) were two infiltrated lymph nodes the size of peas; general icterus; man 41 years old; ¾ nat. size.

tryptic pancreatic necrosis appears very quickly, and what has been said under fat necrosis may be repeated for pancreatic necrosis. Various lesions, mild and severe, create the circumstances for diffusion of the enzymes, and it is a frequent disease if the mild cases are counted. Only exceptionally, the subepicardial, subpleural (Chiari) and subcutaneous fats are involved (Berner, opposed, Heyde). This is also true of animal experiments (see Opie).

If we omit the animal experiments, which give constant results (see above, and p. 1027), the action of steapsin is demonstrated equally well by the rare cases of (*a*) traumatic rupture of a healthy pancreas (Fitz, Simmonds, M. B. Schmidt, Hahn, Selberg, Roosen-Runge and others, see lit. by Guleke), from direct injury (stab and shot wounds, Gobiet, lit.), or indirect trauma (abdominal contusions, subcutaneous rupture, see lit. by Reichle); secretion escapes and fat necrosis of the peritoneum results. The author observed two such cases, one after a knife wound into the pancreas, and one in which a wagon wheel had passed across the body. Activation of the pancreatic juice occurs from necrosis of pancreatic cells, or blood, or the entrance of intestinal juice, etc. These cases are hardly inferior in value to animal experiments, and might be supported by others such as: (*b*) a case of the author; in a 25 year old, very adipose woman, heavy drinker, with a cicatricial pancreatitis of the head, concretions in the duct of Wirsung, occlusion and ectasy of a side branch, a recent abscess the size of a cherry compressing the opening of duct produced a fibrinopurulent peritonitis. The omentum was thickly strewn with opaque, rounded and angular nodules, some several millimeters thick and sharply demarkated, like hard inclusions to the touch; they were most numerous, almost resembling a layer of mortar, in the neighborhood of the gland. The latter was firm and gray, hemorrhagic in a few places; the duct of Wirsung and its branches were filled with cloudy, light gray, viscid mucus. In such cases, the factor of secretion stasis is very plausible, but it is also plausible in other cases of considerably milder degree (*c*) in which icing or map-like spots are seen both on and in the pancreas with mechanical conditions favoring congestion (and diffusion) of secretion, or ascent of duodenal contents or bile. Among these conditions are (1) compression or distortion of the duct of Wirsung, especially frequent in primary carcinoma, chiefly of the head of the pancreas or secondary carcinoma of the pancreas, the gall bladder, the duodenal papilla (fig. 505), the common or hepatic duct, the portal lymph nodes. Other intraabdominal tumors, *e.g.*, a sarcoma of the transverse mesocolon the size of a child's head may supply the necessary condition, or hydrocholecystitis (p. 1000) or, as the author mentioned in the second edition (1901) (and reported by others—Opie, Japha, cf. v. Haberer, lit.) cholelithiasis (if a calculus remains in the papilla, bile may enter the pancreatic duct). Another mechanical condition favoring stasis is (2) occlusion of the duct of Wirsung with viscid mucus which is not rarely discolored by bile for some distance. The author has frequently seen this condition in cardiac lesions, cirrhosis of the liver, emphysema, and similar diseases which inaugurate catarrhal changes in the stomach and duodenum.

There do occur cases (*d*) with isolated foci in which explanation is often impossible. It is probably better to think of causes like those which produce more numerous necrotic foci, rather than to assume some sort of change in the internal secretions. Primarily these foci are not due to bacteria, but bacteria may be secondary invaders (Wolpiansky).

At first glance, things seem more complicated when extensive fat necrosis occurs (*e*), and when the pancreas exhibits an acute hemorrhagic pancreatitis or hemorrhagic necrosis as described on pp. 1026 to 1029. The process in the pancreas may be completely obscured by exudate or adhesions whereupon the opaque gray and yellow white foci of fat necrosis on the omentum and elsewhere indicate the state of affairs.

There still remains a small number of cases (*f*) in which the fat necrosis itself is of greater pathological importance, indeed may even cause death. These are those in which a more vigorous reactive inflammation develops around the small, and isolated foci. While the reaction in the neighborhood is usually relatively slight and more of a reparatory character (p. 1027), in certain unusual cases a more active hyperemic, hemorrhagic, or purulent zone develops around one or more foci with the formation of an abscess; if this is located superficially, it may rupture and lead to local or general fibrino-purulent peritonitis. In most of these cases the colon bacillus is found as a secondary invader from the intestine. Bacteria are not the primary causes (Balser, Ponfick and others) (Eug. Fraenkel, Marx). But it is doubtful that foci of infected fat necrosis can cause an acute hemorrhagic pancreatitis by progressively enlarging, destroying, and liberating trypsin; at least this is the opinion of the majority of recent investigators (cf. Katz, etc., and lit. to p. 1042).

Formation of Pancreatic Calculi

(Pancreatic Lithiasis)

The pancreatic duct and its branches may contain calculi, but they are usually found accidentally in the cadaver. The calculi vary from microscopic size to grains of sand and to walnuts; they are rarely smooth, more frequently nodular (fig. 261, p. 596), mulberry-shaped or cylindrical, sometimes branched, occasionally facetted, as a rule, white, some are brown. If composed of organic masses, they are soft, but are more frequently hard, and usually multiple, up to hundreds. Hard calculi consist of an organic framework and chiefly calcium carbonate and calcium phosphate. They may develop during and as a result of catarrh of the ducts with subsequent stasis of secretion. The consequences of calculi are atrophy of gland parenchyma, fibrous induration of the organ (diabetes in about 50% of cases), suppuration, abscess formation, ectasia of the duct, cyst formation (see under cysts, p. 1049), sometimes fat necrosis (see the case mentioned, p. 1042, also observations of Dieckhoff and Welch). Cholelithiasis and pancreatic lithiasis may be combined (Fuchs). Exhaustive literature by Mockel.

Tumors and Cysts of the Pancreas

Benign tumors are rare. Lipomas, myxomas, chondromas occur. A pedunculated fibroma described by Korte is unique. Lymphangiomas were seen by Koch and by Harbitz; the latter described a retroperitoneal cystic tumor as large as a man's head. Rare adenomas (Rollet) and cyst adenomas with albuminous contents, without specific pancreatic tissue have been observed (Cesaris-Demel), among them papillary cyst adenomas (Soprana, lit.). In some cases, the adenomas were considered a derivative of the islands of Langerhans (Rollet); they were sharply demarkated in a fibrous capsule (Cecil, lit.; Alezais and Peyron, H. Schmidt, Heiberg, Rollet, Koch). The observation of the author presented in fig. 506 is a small-cystic cyst adenoma reported in the Diss. of Basle by Wyss (lit.)

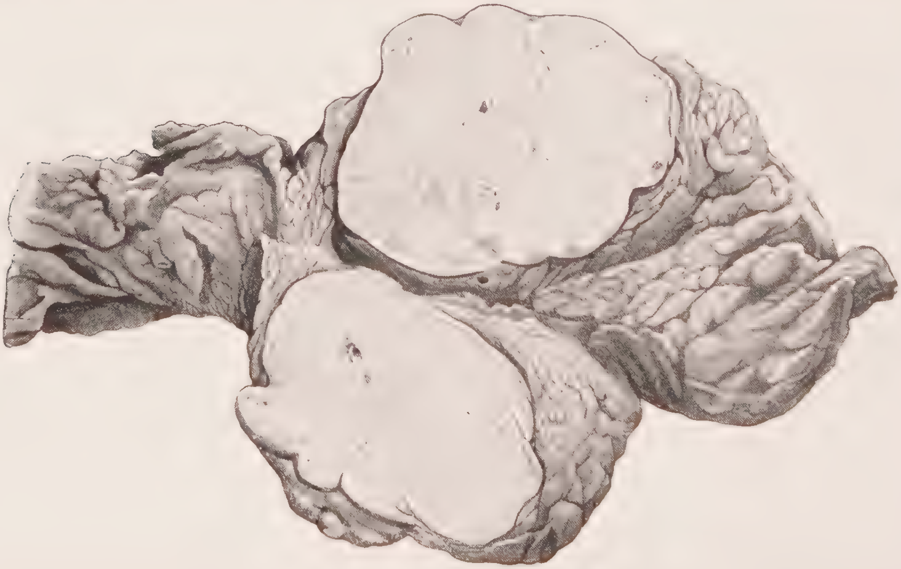


FIG. 506—Cyst adenoma of pancreas of woman 64 years old; almost nat. size; (description and micros. illustrations by A. A. Wyss, I-D, Basel, 1904).

(see lit. by Lazarus, Edling, v. Beust, Roman, Yamane, exhaustive lit.). In a 42 year old woman the author saw a papillary cyst adenoma, parts of which showed carcinomatous change; the cyst, almost as large as a fist, was located in the tail, and a part was forced into the spleen; metastases of a solid scirrhous type were found in the liver and omentum. (Consult cases of Edling, Sotti, Prosorowsky.) [According to Warren, adenomas of the islands of Langerhans are not as rare as the small number of reported cases would indicate. He describes four new cases, bringing the total up to 20; Am. J. Path., 2: 335, 1926.—*Translator.*]

Malignant Tumors.—Sarcomas, mostly round cell, but also spindle- and giant cell (van Rijssell), lymphosarcomas (Ligneris, lit.), endotheliomas (Tancre) are very rare; they appear at any age, and grow diffusely, or as nodules. According to Ravenna, the gland tissue reacts with a cirrhotic process, while Constantini (lit.) believes the tumors themselves may arise from this connective tissue (lit. by Korte, Ehrlich, L'Huillier, Weil, Schirokogoroff, Ssobolew, v. Halasz, F. Albrecht). In a 56 year old man, the author saw a spindle cell sarcoma. Metastatic sarcomas, especially melanotic types, are occasional. Secondary carcinomas are more common by continuity from the surroundings (stomach, duodenum, bile ducts, gall bladder), sometimes through carcinomatous lymph nodes, or by hematogenous routes from a distant focus in the breast, bronchi, prostate, etc., for instance, the primary carcinoma of the pharynx, p. 824.

The most important tumor of the pancreas is primary carcinoma. It usually begins after the 40th year, and may be accompanied by pain in the epigastrium and digestive disturbances, (fatty stools).

The author saw a carcinoma the size of a bean in the tail of the pancreas with numerous metastatic nodules in the liver (3300 gms.), and carcinomatosis of the pulmonary lymphatics; microscopically this was a carcinoma solidum with medium large cells (19 year old girl). A man of 27 developed immense lymph node metastases around the carcinomatous head of the pancreas, on the peritoneum, the liver, the vertebrae, ribs and left supraclavicular nodes.

According to the material at Basle, pancreatic carcinomas comprise 1.76% of all carcinomas (other statistics by Fuchs).

Harder and softer forms are found, the former more frequently. There are combinations of both; the softer parts appear roughly acinar, like pancreatic tissue, but whiter. It is conceivable that cirrhosis is sometimes a predisposing factor in the development of the neoplasm (Hulst). According to the point of origin, the cells are (*a*) rounded angular, suggesting gland cells, or polymorphous, with nuclei rich in chromatin, or like the cells of the islands of Langerhans, from which, according to Fabozzi, most carcinomas of the pancreas are derived. This statement, however, needs proof in its general application; as Gelle points out, adenocarcinoma would be difficult to understand; actually, the islands are quite resistant to invading carcinoma and may be replaced by regeneration, a fact which explains the non-appearance of glycosuria, even when the whole pancreas is infiltrated by the tumor (A. Heiberg, Grimani, Ravenna, Herxheimer and others). [Wilder, Allan, Power and Robertson (J. A. M. A., 89: 348, 1927) report a carcinoma arising in the islands of Langerhans accompanied by hyperinsulinism and hypoglycemia.—*Translator.*] (*b*) The cells are cylindrical or high cylindrical, corresponding to the epithelium of the intralobular and interlobular ducts from which they may be derived (Hulst, Ssobolew, Koch). The large ducts at times show predisposing epithelial proliferations due to inflammatory processes. Names applied are solid simple carcinoma and adenocarcinoma, sometimes papilliferous. The former are much more frequent. Mucoid carcinomas are rare, but the author saw a mucoid adenocarcinoma the size of a fist in the head of the pancreas of a 52 year old man. It has not been proved that the small mucous glands which accompany the main duct and its larger branches can originate a carcinoma. The squamous cell types and combinations with the adeno types (metaplastic carcinomas) are rare; it is important to remember that metaplasia of the cylindrical epithelium of the ducts into pavement epithelium can occur without a tumor (Kawamura, lit., Papadopoulos). Anderson described a psammo-carcinoma. In a case at Basle, a solid scirrhous cylindrical cell carcinoma (male 70 years of age) was in the head of the pancreas. It was a nodule the size of a hen's egg and in it were many veins filled with tumor cells. In spite of this, there were no distant metastases; only some lymph nodes in the vicinity of the head of the pancreas were infiltrated to the size of cherries.

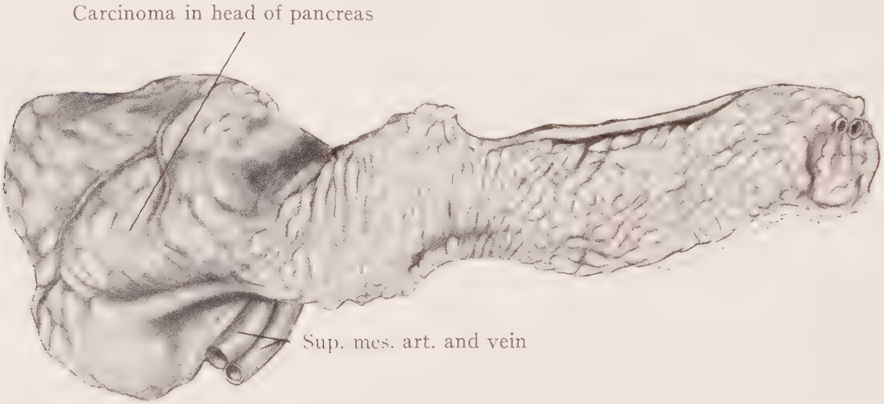


FIG. 507.—Carcinoma of the head of the pancreas. In a patient 52 years old. This is the type growth which notoriously produces obstruction of the bile ducts. L. H. #211. ½ nat. size.

The extension of carcinoma may be diffuse; the entire organ is enlarged, or, more frequently, diminished in size and indurated, sometimes with the formation of small isolated cysts; or the tumor may be confined to the head of the pancreas; this is more frequent; the tail alone becomes tumorous in but few cases.

In 35 cases of K. A. Heiberg, the carcinoma was confined to the head in 23 cases, while in 5 cases the whole pancreas was involved. See statistics by Leriche.

A carcinoma of the head of the pancreas may be larger than a hen's egg, indeed as large as a fist or more, but sometimes they are small enough to be overlooked. Enlargement of the head is frequently helped by carcinomatous lymph nodes, intimately and indistinguishably fused with the tumor. Consequences may be: dilatation of the duct of Wirsung; secondary obstructive jaundice from distortion, compression, obstruction or infiltration of the common duct (marked dilatation of the bile ducts and the gall bladder!); simple or carcinomatous thrombosis of the portal vein, congestion of the portal system (splenic tumor, ascites); ileus from compression of the duodenum (case, p. 714) by adhesions to the tumor, or stenosis from scirrhous infiltration of its wall. In a 79 year old man with a carcinoma of the head of the pancreas the size of a small walnut, the author saw circular infiltration of the adjacent bowel. Rupture into the duodenum also occurs, (easily mistaken for primary duodenal carcinoma!) or into the stomach. The most frequent metastases are in the nearby lymph nodes and the liver (50% in the material in Basle, p. 965). A tumor as large as a goose-egg was found in the tail of the pancreas (57 year old man); the liver was filled with nodules and weighed 4485 gms., (the author). But in a 31 year old woman with a small hard solid carcinoma in the head of the pancreas, the metastases were in the 10th and 11th thoracic vertebrae and in the spinal dura causing compression of the cord; the lymph nodes were free (!), and the liver contained only a few small nodules (the author). Metastases may appear in many other places, as in an observation of the author who found, in a 55 year old woman with diabetes, a diffuse scirrhous solid carcinoma in the head and middle portion of the pancreas with bile obstruction and marked fat necrosis and metastases in the left supraclavicular nodes, the 10th. thoracic vertebra and the left kidney. Sometimes it takes very searching histological examination to distinguish a carcinoma of the papilla of Vater from a carcinoma of the head of the pancreas.

Cysts of the Pancreas

Cysts of the pancreas are: (1) rare cystic adenomas and lymphangiomas, so-called proliferation cysts; (2) dysontogenetic cysts (Wegelin, Yamane, lit.) as in the congenital cystic pancreas which appears alone, or very rarely with cystic liver and cystic kidneys, (the author, Glang, Hennig, v. Meyenburg, Yamane). These are probably due to snaring off of small ducts in early embryonic life; they are malformations, and the retention is a secondary matter. (3) True (acquired) cysts are lined with epithelium and are usually from retention. (4) Cystoids or pseudo cysts, not lined by epithelium are the most important pancreatic cysts from the clinical viewpoint, since they can be removed successfully by operation (Korte, Lazarus, Steinel and Mandl, Yamane, lit.).

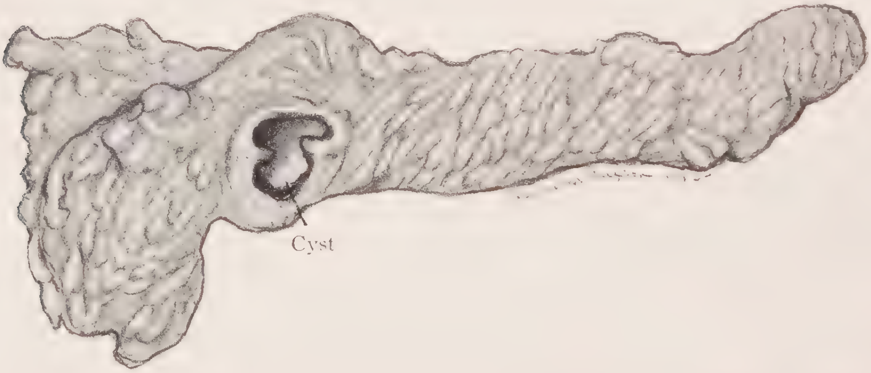


FIG. 508.—Small cyst in the body of the pancreas. Sketch made at operation. The fluid slightly cloudy and contained a trace of a protein-splitting enzyme. The sac was opened, packed with gauze and the patient recovered. L. H. ½ nat. size.

Retention Cysts. If the opening of the pancreatic duct is occluded by a calculus or tumor, and if the character of the secretion, and if the absorptive ability of the lymph vessels has been changed, *e.g.*, by cirrhosis of the pancreas (Senn, Lazarus and others), the duct dilates cylindrically, saccularly or like a rosary; the ectasia may reach the size of a child's head or more (solitary retention cysts). In animals, after ligation of the pancreatic duct, secretion continues for some time and causes dilatation of the duct (Heidenhain); later the secretion is absorbed, but not excreted by the urine (Kuhne). Finally the gland atrophies and undergoes fibrous contraction (but not autodigestion!), but the islands of Langerhans remain (see p. 1035), even enlarge and multiply, so that diabetes does not develop (W. Schulze, Gontier de la Roche, Herxheimer—Moldenhauer (lit.), Gelle (lit.), Massaglia and others). Sometimes the cyst formation is unimportant, multiple, perhaps numerous (cystic degeneration), confined to small ducts or even to one acinus; these are usually due to indurative interstitial inflammation or to concretions. The small cysts may contain butter yellow, thick, fatty, and at times mortar-like calcified, and rarely gelatinous material (von Loghem).

Scota reported carcinomatous and sarcomatous degeneration.

Cystoids are solitary, large, to immense, globular pouches, usually situated in the tail, though the author saw them in the middle portion of the pancreas; their contents are mostly sanguinous, occasionally almost colorless or gray to black. As a rule, they have no connection with the ducts of the gland. Indeed their relation to the pancreas is often difficult to recognize since the cysts grow more and more independently above it.

Large cysts may grow retroperitoneally between the stomach and transverse colon, or between the stomach and liver, or below the colon.

Some clinical pancreatic cystoids are in reality not pancreatic cysts at all, but cysts of adjacent structures; consult p. 1050 for differential diagnosis.

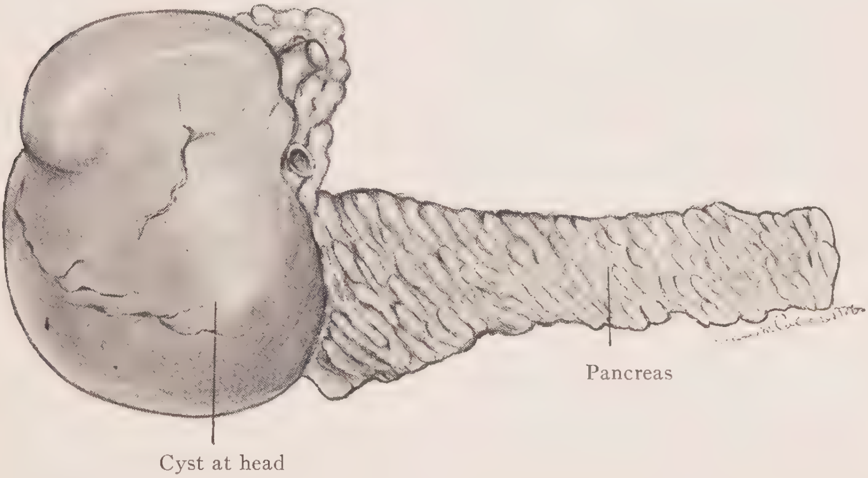


FIG. 509.—Large cyst at the head of the pancreas. Sketch made at operation. This cyst was opened, a slightly turbid fluid removed, its walls everted and the patient recovered. Its etiology is problematic. The fluid contained within the cyst contained no enzymes. L. H. ½ nat. size.

In reference to the etiology, there is much diversity of opinion. Friedreich thought cyst formation was due to primary hemorrhages (hematomas), and he contrasted these apoplectic cysts with retention cysts into which hemorrhages have occurred. Hemorrhage of traumatic origin may produce cysts filled with serous fluid and with walls of cicatricial, rust colored tissues which often have an inward shelving character (traumatic blood cyst), (lit. by Lazarus and Honigmann, Luxembourg, Duschl; in reference to trauma of the pancreas generally, see Guleke). Traumatic ruptures lead to activity of the pancreatic juice, and blood and juice pouring into the omentum produce a hematoma, which by reactive granulation tissue growth and transformation of its contents, becomes a pseudo cyst of the omentum. In other cases, secondary hemorrhages take place into changed tissue. Probably the most frequent primary lesions are the necrotic hemorrhagic foci of acute pancreatic necrosis; the process of formation of these pseudo cysts has been described on p. 1027. It has been stated, p. 1026, that foci of fat necrosis have no such importance. Other authors are of the opinion that an interstitial pancreatitis prevents prompt absorption by lymphatics, so that there is congestion of secretion with autodigestion and subsequent small cystic cavities; in these, the hemorrhages are secondary to vessel erosion (as in gastric ulcer), (Tilger). It is yet to be proved that this process is at all frequent.

Microscopical and chemical examinations of the cyst contents have given no uniform results. In a number of cases, they contained demonstrable diastatic and fat emulsifying substances (comp. p. 1026), in other cases serous, or sero-sanguinous, or purulent, or hemorrhagic materials. With hemorrhagic contents, there have been found also numerous granules and globules.

In the differential diagnosis there must be ruled out cyst formation in the omentum from lipomas which undergo central liquefaction, or from softening and hemorrhage in carcinomas, cystic changes in mesenteric lymph nodes (Rokitansky), or cystic tumors, for instance, chondromas of the spine (rare). Consult for pancreatic cysts, Lazarus (lit.), Guleke, F. Albrecht (lit.), Steindl (lit.).

Parasites.—The hydatid echinococcus is quite rare (lit. by Frankenheim, Hanser), as are ascaris (foreign body tubercles due to wandering ova, see Muroya) and distoma (Seyfarth, lit.). Cysticercus may be imitated by Vater-Pacini bodies, which are white, vesicle-like structures the size of a lentil and may cover the pancreas quite thickly (Ceelen, lit.).

CHAPTER V

DISEASES OF THE OSSEOUS SYSTEM

General Remarks on Bone Resorption and Bone Formation

[For discussions see Reports of Progress in Orthopedic Surgery published in Arch. of Surg. each year.—*Translator.*] In spite of the firmness and rigidity associated with the bones, and in spite of the apparent unchanging composition of completed osseous tissue, there is a physiological progressive internal rearrangement, a never ceasing change in the rigid columns, not only in the growing individual (v. Ebner), but even into old age (Pommer). On the one hand, there are destruction and resorption of the finished bony tissue, and, on the other hand, there is replacement by new osteoblastic tissue, at first without calcium (osteoid), but under normal conditions, soon with calcium.

These processes may occur simultaneously in one and the same bony trabeculae. This oft-repeated accession of new bone in the spaces produced by resorption of the old, does not always conform to the old lamellae, and thus is produced the characteristic microscopic appearance of the bones of adults, *i.e.*, of wavy lines, closely bordering each other, of various forms, with variously oriented lamellar systems.

In the growing skeleton of youthful individuals, particularly children, these resorptive and replacement processes lead in a relatively short time to total new arrangement of the skeleton, while in adults this combination is much less in intensity; in old age, as a rule, destruction is greater than growth. Under pathological conditions, resorption of completed bone and formation of new osseous tissue is quite frequent, and easily stimulated.

What Processes are at Work in the Resorption of Osseous Tissue?

(*a*) *Lacunar resorption and smooth resorption; lamellar spaces*, (*b*) *the formation of perforating canals*, (*c*) *their disappearance after previous removal of calcium* (*osteomalacic bone disappearance*).

(*a*) The most frequent method by which completed bony tissue is removed, is by lacunar resorption. This process occurs not only physiologically, but very frequently pathologically, *e.g.*, in the various forms of atrophy, particularly pressure atrophy, in diminishing the size of a callus, the removal of sequestrae, on the surface of ivory transplants grafted into the living bony tissue, etc. On the smooth surface of the bony substance, there appear ovoid or shallow burrow-like depressions—the so-called Howship lacunae containing small cells which cannot be differentiated from osteoblasts, or large, many-nucleated, giant cells (osteoclasts Kolliker), obviously concerned in lacunar solution, and differing entirely from the bone marrow giant cells (figs. 510, 511). The osteoclasts are not specific cells, but offsprings of the connective tissue, especially of the endosteum; moreover, the most varied kinds of pathological cells which lie close to the bone, such as granulation tissue, tumor cells, etc., may become osteoclasts. Many believe vessel buds from overgrown vessel endothelium may also give rise to these cells, see p. 574. Structural changes in the bony substance indicating primary removal of the calcium (Kolliker) are not present (Pommer); in addition to their mechanical effect—pressure—(Wegner), the giant cells probably exert a chemical function also. But the discovery of a lacuna does not necessarily indicate the previous activity of osteoclasts (von Recklinghausen). By confluence, the lacunae become larger spaces. By the time resorption has ceased, the giant cells can no longer be found; perhaps they then become fibroblasts.

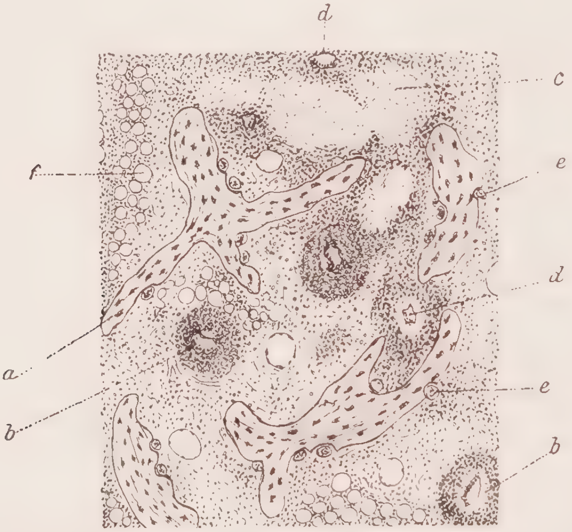


Fig. 510.—To demonstrate lacunar absorption: tuberculous caries of a tarsal bone; a, bone trabeculum; b, tubercle, caseous center, epithelioid and giant cells; c, caseation in tuberculous granulation tissue; d, giant cell in tubercle; e, osteoclasts, some in Howship's lacunae; f, fat-containing bone marrow; in other places wide, delicate walled veins in bone marrow (med. magn.).

It should also be remembered, that just as there is lacunar absorption with, or without giant cells, there may also be resorption without lacunae or osteoclasts; this has been aptly described as smooth resorption (Busch). Richly cellular connective tissue, as well as tumor cells, the latter particularly, produce these changes.

This process is entirely different from that described by Ernst and v. Muralt, as lamellar separation, as seen occasionally in tumors. The cells invade between the bony lamellae, which retain smooth edges, but become more and more fragmented, until finally a very fine polymorphous bone sand remains, which is eventually completely resorbed.

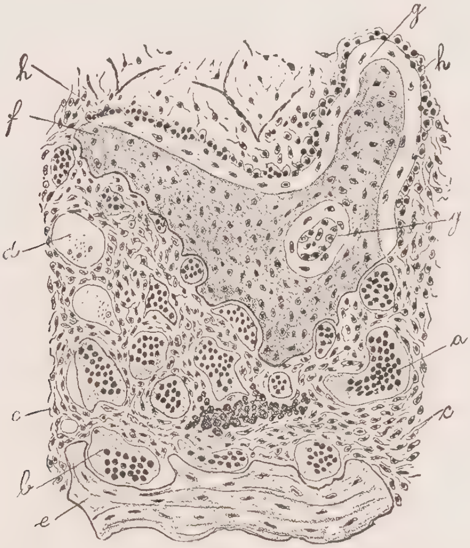


FIG. 511.—Bone absorption and new formation in osteofibrosarcoma gianto-cellulare of the ulna; a, giant cell; b, giant cell in a Howship's lacuna (osteoclast); c, fibrosarcomatous tissue, fibrous, giant- and spindle-cells, in center of illustr. brown blood pigment; d, blood vessel; e, old bone trabeculum; f, new-formed bone; g, bone margin still uncalcified formed by osteoblasts h. (High power.)

(*b*) **The Formation of Perforating Canals (Canalization).**—The second kind of bone resorption, seen under physiological conditions, at least, to some degree, is by means of perforating canals (resorption canals, or the so-called Volkmann canals), which destroy the organic part of bones. Under physiological conditions, these are canals of varying number, containing vessels (perforating vessels); they come partly from the periosteum, partly from the medullary cavity, and partly from the Haversion canals; they bore through the bony lamellae, helter-skelter, in all possible directions, and therefore are not like the Haversion canals which are surrounded by annular lamellae, and are much larger. Under pathological circumstances, the conception of these perforating canals is carried further. We speak of Volkmann's canals when vessels with buds (Pommer), or vessel-containing connective tissue, with, or without, osteoblasts, come from the medullary space of the substantia spongiosa, or from a Haversion canal of the compact substance, and bore through the lamellae into another medullary space or another Haversion canal, and thus produce a tract which naturally may occasionally open one or another of the bone corpuscles. (Bone tissue occurs in two forms: (*a*) the spongy substance consisting of a meshwork of bony spicules and plaques between which there is marrow and (*b*), the compact substance, the rigid structure of which contains the blood vessels in the Haversion canals, which empty externally, as well as internally, toward the spongiosa.) The term "Volkmann's canals" also includes irregular, ampulla-like dilatations of bone corpuscles, *i.e.*, cavities, (illustrations under osteomalacia, p. 1076), and spaces formed by the confluence of such dilated bone corpuscles, or irregular, angular canals which penetrate the bony substance, and which, when they have opened into a medullary space, may even be filled with cells (p. 1076, illustration IIe); these canals are dilated still more by the osteoclasts, but, on the other hand, may be so clothed with concentrically laminated bone by the osteoblasts, that they become similar to Haversian canals, or even obliterated. Axhausen (lit.) believes all Volkmann's canals are preexisting vessel paths closed in by the laying down of bone, and recognizes lacunar erosion as the only form of destruction; see also Fujii, Lotsch and v. Recklinghausen.

(*c*) **Disappearance of Bone Following Previous Removal of Calcium; Osteomalacic Bone Disappearance.**—Under much rarer circumstances, *e.g.*, in senile, marantic, and the so-called puerperal or non-puerperal pure osteomalacia of women, the disappearance of bone occurs in such wise that the calcium is removed first (halisteresis); the remaining bony ground substance (bone cartilage), is then dissolved, during which process it may temporarily appear fibrous. Definite destruction and resorption of the decalcified, fibrillar bone then occurs, as a rule, without osteoclasts. v. Recklinghausen conceived that in addition to halisteresis, thrypsis also takes place, *i.e.*, slowly progressive softening, first resolving the bony substance into its elements, and afterwards, liquefying it. The decalcified borders of the bony trabeculae appear as red streaks after simple staining with carmine, or double staining with hematoxylin and neutral carmine (or eosin), (so-called osteomalacia seams); the calcium-containing bone stains blue.

To avoid mistakes, it must be remembered that newly formed osteoid tissue (that containing no calcium, as yet), also stains red with carmine or eosin. Under the heading, osteomalacia, there are more details concerning the differentiation of decalcified old, and non-calcified new bone (p. 1074).

In handling fetal bones for microscopic examination, it is advisable to use celloidin embedding of completely uncalcified bones, and staining with hemalum-carmine. For the bones of older individuals: decalcification with Muller's fluid, frozen sections, staining with hemalum-eosin, which in relation to the distribution of calcium, gives just as good results as in undecalcified material. See also Pegger, Dibbelt.

The formation of lattice figures (v. Recklinghausen) as a particular form of the disappearance of calcium (p. 1076, illustration III). Complete removal of calcium (halisteresis) is a peculiar change occurring frequently under various circumstances, not only in classic osteomalacia, but also in bone resorption from destructive tumors (Apolant) and other conditions. The peculiarity lies in the appearance of newly formed, (not preformed), reticulum-like figures in the bony substance, which take on many contours, and which are occasionally quite obvious; when they are injected with air or with carbon dioxide, and examined microscopically with transmitted light, following total reflection, they remain dark, or gray black, and thus are easily seen. They depend upon resorption of calcium, and at first, follow the course of the interfibrillar spaces. Thus the ground substance of the bone is divided into its elementary parts, *i.e.*, into the fibrillae. (Analogue: Asbestos-like degeneration of the cartilage.) These figures are seen best in sections of osteomalacia material, which have not been preserved in Muller's fluid long enough to become entirely decalcified, or in preparations hardened in alcohol, according to the methods of v. Recklinghausen (and Apolant), in which air or carbon dioxide is injected into the finer spaces. It is then seen that the figures, even though not without exception, nevertheless with preference, appear in the lacunar contorted transitions of completely calcium-less and calcium-containing internal parts of the bony trabeculae, *i.e.*, where the decalcification is proceeding; this transitional zone is characterized by granular, brittle stripes in preparations which have not been injected with air or carbon dioxide. The distribution of the figures is not particularly regular nor equal, rather in foci without any relationship to the normal architecture. The same figures are also seen in the internal parts of the calcium-containing bony substance in osteomalacia. In completely decalcified (osteoid) tissue, on the other hand, they are no longer present; the interfibrillar spaces are closed in this case by the closely applied fibrils which become hyalin, swollen and fused together.

In opposition to v. Recklinghausen's idea of these reticula, Hanau has expressed the opinion that they are new deposits, and recently, Pommer has pointed out, that they are probably incomplete granular deposits of calcium; M. B. Schmidt, however, believes that the objections of Hanau (Bertschinger) are without point. Schmorl, Looser (lit.) and Axhausen (lit.) deny completely the importance of these figures as signs of halisteresis; they even believe that some of them are artefacts (Pegger-Pommer).

On the other hand, v. Recklinghausen, in a comprehensive work, has again demonstrated the validity of these peculiar structures (agreed to by M. B. Schmidt), and that destruction by halisteresis really does occur in preformed bony substances as well as in rickets. Dibbelt vigorously defends the idea of halisteresis; see also Jores, Schloss. It is probable that these figures should be recognized as the expression of incomplete calcium content.

Observations Concerning the Normal Structure of Bony Tissue.—(Details by Schaffer.) The ground work of the bone is not homogeneous, as might be thought on first microscopic observation, but as in other connective tissue substances, it has fibrillae, gelatin-giving fibers (v. Ebner), which, in lamellar bones, lie practically parallel to each other, and are tightly bound together by rigid cement substance (Kolliker doubts its existence) containing calcium salts; the structure is very fine and the bone fibrillae assume a stratified perpendicular arrangement. In nonlamellar bones preexisting, much heavier fibers are the connective tissue matrix—the so-called Sharpey's, or perforating fibers—and produce reticuli, some of which are calcified but the majority uncalcified; the fibrillae intermesh among themselves quite irregularly. Therefore, we may differentiate: finely fibrillar (lamellar),and roughly fibrillar (reticulum-like) bony tissue. The calcium salts in both the ground substance and the interfibrillar connective substance, are chiefly basic phosphoric acid salts, with smaller amounts of the phosphoric acid salts of magnesium.

The ground substance contains elongated bone cavities (bony lacunae), in which are embedded flat-oval bone cells (octeocytes) with prolongations; these lacunae and cells are known as bone bodies; the bony lacunae and the bone cells in reticulated bones are larger, more irregular in contour and arrangement, and are often coalesced. The lacunae are connected by delicate, many-branched communications. The immediate neighborhoods of the latter are chemically and physically different; capsule-like condensations surround these spaces, the so-called marginal sheaths (Broesike; for more details see Schaffer). The bony canals empty into the Haversian canals as well as on the external and internal surfaces of the bones.

In adults, the entire skeleton shows finely fibrillar lamellar bone, which is formed by osteoblasts; its ground substance (in contrast to the reticulated bone) contains elastic fibers also; the finely fibrillar mass itself is not preformed and closed in mechanically, but is a product of the activity of osteoblasts (see next chapter). In childhood, Sharpey's perforating fibres penetrate a portion of the lamellar bone, *i.e.*, the external general lamellae (called by others, ground lamellae), which run along the outer bone surface—in contrast to the internal, which run along the inner surface—and the irregular interstitial lamellae, which lie against the external lamellae and between the Haversian system; these fibres of Sharpey are of connective tissue running in various directions in the bony substance and boring through it; some are calcified and some remain uncalcified. They are, however, confined to the periosteal portion, and are not present in mature bone. The Haversian or special lamellae, rings placed concentrically around the Haversian canals, first produced by osteoblasts working from inside of the canals, also lack Sharpey's fibers.

The roughly fibrillar reticulated bony tissue is very plentiful in embryonal bones, particularly in the periosteal, *i.e.*, perichondral, and the secondary (connective tissue) bones; but, from the first year of life onward, the ground substance of the connective tissue bones (vault of the skull, lateral sides of the skull, almost all the bones of the face), becomes finely fibrillar (lamellar), *i.e.*, replaced by osteoblastic bone, in greater and greater mass, so that by maturity, roughly fibrillar ground substance is found normally only along the sutures, and the insertions of the tendons. During this replacement process the reticulated bone is made to disappear by resorption; this produces many irregular wavy spaces, the so-called Haversian spaces, which are an indication of youthful bony tissue, and which later, through the deposit of lamellae, become Haversian canals. On the other hand, reticulated ground substance is frequent in callus and under pathological conditions such as rickets, in which it produces enormous periosteal layers, and the marrow osteophytes; the bones so built are characterized, first as youthful, and second, as produced from a connective tissue matrix.

Lamellar bone is produced by osteoblasts; reticulated bone, on the other hand, from connective tissue, *i.e.*, from ground substance and cells; the former undergoes calcification.

What Processes Occur during Pathological New Bone Formation?

Pathological new bone formation occurs in exactly the same way as physiological new growth.

The marrow, periosteum, cartilage, and, with restrictions, the connective tissue, are bone-forming structures. The actual bone producers are the osteoblasts, and their points of origin are the periosteum and the endosteum of the marrow. The connective tissue and the cartilage are more limited in their importance; the latter is frequently replaced by bone, but usually only indirectly, after previous resorption, and seldom directly, *i.e.*, metaplastically to bone.

The endosteum consists of a fibro-cellular structure, which clothes all the spaces of the bones, and produces, at the same time, the vascular and connective tissue framework, enclosing the specific bone marrow parenchyma in its meshes. The endosteum serves to produce the new bone of the skeleton, as well as bone resorption (Ssamoylenko, lit.).

New bone is formed in various ways:

(*a*) From the apposition of osteoblasts to completed bony trabeculae (p. 1060, illus. I and II). These cells come from the connective tissue of the inner layer of the periosteum (cambium layer—osteogenetic layer, periosteal marrow of Ranvier), as well as from the marrow, but more accurately, they are a particular part of the marrow, the endosteum, which is genetically like the periosteum, and is in uninterrupted communication with the latter (fig. 512). The osteoblasts lie along the older trabeculae somewhat like polymorphous epithelial cells with fine prolongations; they increase in number by nuclear division. After their nuclei disappear, they change into a homogeneous-appearing, but actually fibrillar, ground work, which becomes lamellar bone after calcification; but some of the peripheral protoplasmic layers become ground substance, in which, then, the center is enclosed as a bone cell in an angular cavity with prolongations. These cell cavities are called "bone bodies." (For staining with their prolonga-

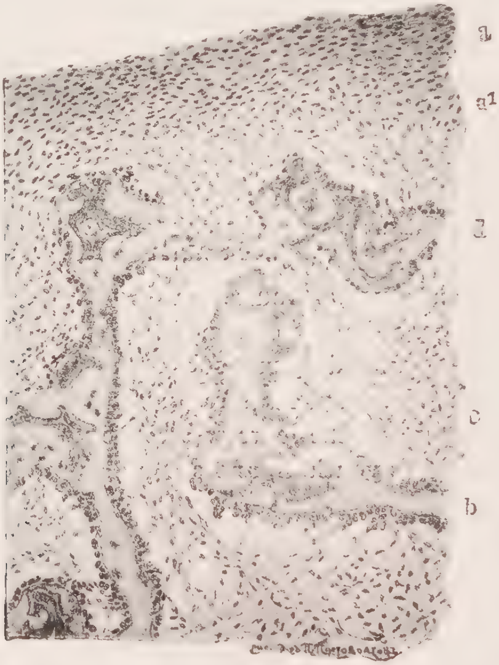


FIG. 512.—Endosteum in active condition, diaphysis of femur of an embryo; a, periosteum; a′, its cambrium layer; b, bone columns surrounded by cubical osteoblasts; c, between the bone column the ingrowing periosteum, its structure becoming more loose; d, cartilage, not ossified (high power).

tions—bony canals—according to the method of Schmorl, see Schaffer and Fasoli, lit.; see also the method of Morpurgo.)

(*b*) Whereas, in the above mentioned condition, the osteoblasts produce a more or less thick covering around the complete bone, in another form of bony new growth, the osteoblasts gather together in more or less large foci, and produce masses and trabeculae in the growing marrow (endosteum), *i.e.*, in the growing osteogenetic periosteal layers. The growth of all of the cells of the endosteum and the periosteum is very vigorous, and characterized by much nuclear division. Inside of the masses of large nucleated, richly protoplasmic osteoblasts, arranged in foci and bands (p. 1060, illus. IV), low magnification shows a homogeneous ground substance which, on stronger magnification, is found to be finely fibrillar, glutin-containing, and without calcium (osteoid tissue), to the formation of which some of the osteoblasts are assigned; in other parts, plump rounded, and later angular cavities are enclosed, and thus become bone cells. Osteoid tissue is bone without calcium salts; it forms trabeculae, and the growing marrow tissue fills the interstitial spaces between them. The accretion of calcium salts changes osteoid tissue into completed bone. (For other views concerning osteoid tissue, see Dibbelt.) According to Gierke, Schmorl, Ehrlich, iron accumulates in the ground substance before calcification. Orth considers unimportant the theory which holds that this impregnation with iron salts is a sort of whip for the subsequent accumulation of calcium. Hueck believes that the finding

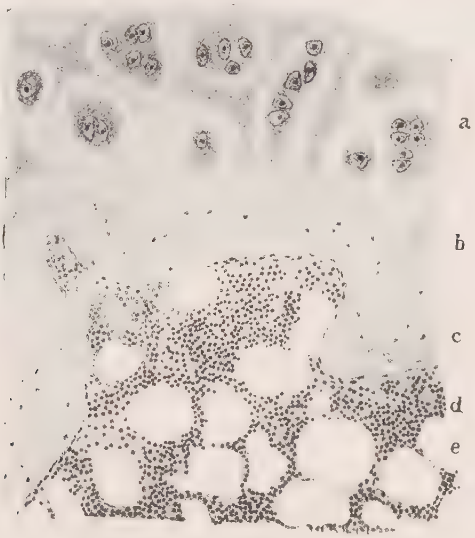
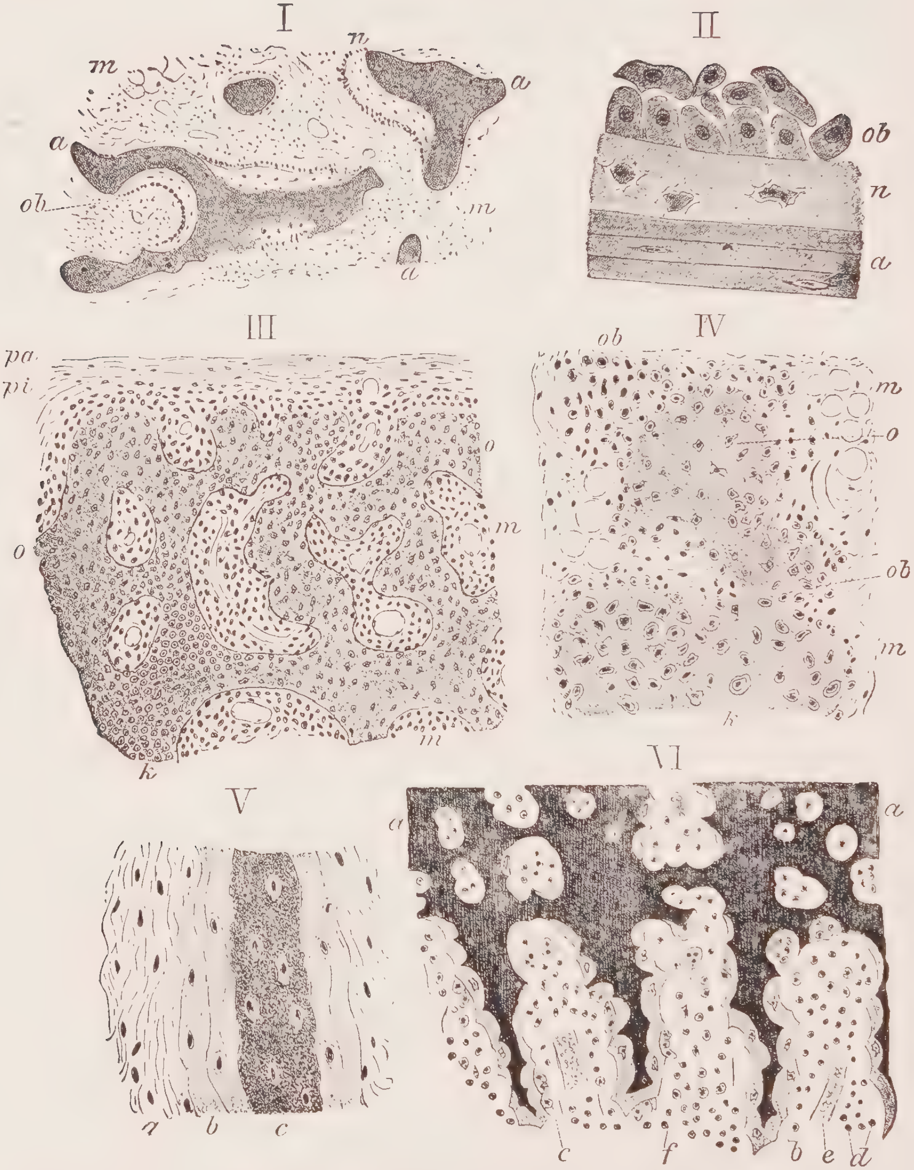


FIG. 513.—Resting endosteum; epiphysis of femur of an individual in middle life; a, cartilage; b, bone; c, the osteoblasts parallel to the bone; d, bone marrow; e, fat cells. (Low power.) (After Ssamoylenki. The endosteum, Virchow's archiv., 211, 1913.)



FIGS. 514–519.—Apposition of osteoid margins by osteoblasts; from the depth of a gummatous niks ulcer penetrating the tarsal bones; a, trabeculae of old calcified bone, deep blue stain; n, newly formed opposed bone edges (osteoid) produced by osteoblasts (ob.) and non-calcified, stained red; m, fibrous marrow; above to left, fat cells; some blood vessels. Hematoxylin (blue) and eosin (red) (low power). II. Bone formation by deposition of osteoblasts (ob.) on old bone (a); n, new bone, not yet calcified (osteoid) (high magn.). III. Formation of osteoid trabeculae from the periosteum from a fracture two weeks old; pa, periostium, outer layer; pi, periostium inner layer, proliferating germinal tissue; o, osteoid trabeculae; k, cartilage tissue; m, germinal tissue which changed into marrow tissue; staining as in I. (Med. magn.) IV. Myelogenous bone and cartilage formation from collections of osteoblasts; from a fracture about 3 weeks old (osseous and cartilaginous marrow callus); k, cartilaginous tissue above changing into bone o; ob, heaps of osteoblasts in marrow tissue m. Stain as in I, somewhat

of iron is an artefact, produced by preserving or hardening fluids containing this substance. But the investigations of Sumita confirm the fundamentals of this "whip" theory of Schmorl (see Eliascheff). Completed bone does not give a Prussian blue reaction (p. 372). The newly formed trabeculae are arranged as in spongy bone. Overgrowth of the marrow tissue may also produce cartilage. See Gottlieb, Broman, concerning vital staining of the calcified tissue by means of feeding "kropp" (a specially prepared grain); in younger animals, fed with "kropp," the bony layers in the course of formation are stained red, because there is produced a compound of calcium alizarine.

The osteoid trabeculae (p. 1060, illus. III), coming from the periosteum, begin in the connective tissue as a cellular (osteoblastic) overgrowth accompanied by new vessels. The germinal tissue thus produced becomes in part, osteoid trabeculae, enclosing many old, tough, fibers (Sharpey's fibers of the connective tissue, p. 1056), and in part, marrow tissue. Through the absorption of calcium, spongy bone appears. Furthermore, following partial resorption, new bony substance may be applied in lamellae by osteoblasts; this may also contain Sharpey's fibers, either calcified or not, and can be recognized as bone developed in a connective tissue matrix (p. 1057). The trabeculae are thus made thicker, the marrow spaces narrower.

(*c*) From direct change (metaplasia) of periosteal or endosteal connective tissue to bone, without cell growth (p. 1060, illus. V). The striped ground substance becomes thickened, sclerosed (Gegenbauer), and has a peculiar sheen (proosteoid tissue); if the cells of the non-calcified connective tissue are enclosed in angular cavities, the structure is spoken of as osteoid tissue. After taking up calcium granules, which later coalesce to a homogeneous mass, this osteoid tissue becomes bone. (Consult this mode of formation under ostitis fibrosa.)

(*d*) The growing periosteum (p. 1060, fig. III), more rarely, the marrow, *i.e.*, the endosteum (p. 1060, illus. IV), may also produce cartilage. Between its formative cells, the chondroblasts, there appears a hyalin, chondrin-containing ground substance; later, the cells lie in rounded spaces surrounded by thickenings, like capsules (Schaffer). There then appears a cartilaginous or chondroid tissue, which is changed into osteoid,

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higher power than III. V. Metaplastic transformation of fibrillary connective tissue into bone, from an ossifying fibrosarcoma almost as large as a man's head from the region of the back, existing 20 years; a, connective tissue; b, thickened connective tissue without calcium (osteoid); c, bone. The connective tissue cells are enclosed in cavities and become bone cells. The osteoid connective tissue calcifies. Stain as in I. (High power.) VI. Endochondral ossification, diagram. Advance of marrow spaces into the calcified basic cartilaginous substance with opening of cartilage cavities. Formation of bone tissue by osteoblasts from the marrow. The bone trabeculae thus formed contain remnants of calcified basic cartilaginous substance (a). Osteoblastogenic bone, c, osteoblasts; d, marrow cells; e, blood vessels; f, giant cells. (High power.)

or into actual cartilage. On staining with hematoxylin, the cartilaginous ground substance becomes red violet to blue violet.

(*e*) The cartilage is changed to bone by its ground substance absorbing calcium salts, (where calcium is present, iron also appears, see above); then vessels and marrow cavities appear. The capsules of the cartilage break open, the free cells disappear (or become marrow cells), the vessels and cells of the marrow invade the spaces. From the marrow, therefore, when osteoblasts arrive (p. 1060, fig. VI), there is formed bony substance, which is laid down upon the walls of the cavities, the calcified cartilaginous ground substance remaining in trabeculae. We will again meet this process in speaking of enchondral ossification. At first, after almost complete disappearance of the cartilage, an osteoid tissue is produced by the invasive marrow, and laid on the remaining cartilaginous trabeculae. Then the osteoid tissue may become calcified, and the marrow (endosteum), may produce more bony substance by the activity of osteoblasts.

(*f*) By metaplasia, the cartilage is turned directly into bone. Cartilaginous bone is irregular, the bone bodies are arranged in groups, columns, or isolated in the ground substance. Normally this chondrometaplastic type is developed but seldom, *e.g.*, in the lower jaw, and, according to Manasse and Shin-izi Ziba, during the endochondral ossification of the petrous portion of the human temporal bone. In rickets, in the ossification of enchondromas, and in the formation of callus, it does play a rôle. Borst is of the opinion that direct metaplasia is improbable, and may be mistaken for an insidious replacement of the cartilage by bone.

Regressive Changes. The Disappearance of Bone from Simple Atrophy, and from Softening (Osteomalacia)

By simple atrophy of a bone is meant disappearance of completed bony structure, not from increased resorption, but, as Pommer showed, from disappearance or diminution of the apposition processes; the resorptive processes continue physiologically (p. 1051).

Thus the size of a bone may be the same, or smaller, *e.g.*, the atrophic lower jaw, an amputation stump, etc.

If disappearance occurs from removal of the calcium and its resulting softening, or if, as others assume, the physiologically removed bone is replaced by soft osteoid tissue, the condition is known as osteomalacia. Disappearance of bone from inflammatory processes is called caries. When bone tissue is destroyed by any process, if, *e.g.*, an extensive destruction of the periosteum produces diminution or removal of nutrition, the condition is known as necrosis. We must differentiate from atrophy: (1) aplasia, caused by a failure of the primitive anlage, and (2) hypoplasia, hypostosis, due to an inhibition of the normal growth.

When lacunar resorption occurs along the outer surface of a bone, and the osteoclasts lie close together and produce large Howship resorption lacunae, the surface of the bone appears rough and furrowed. Larger superficial or deep defects are known as bone ulcers. When lacunar resorption takes place over a larger area of the external part, and the bone becomes quite thin, the result is called concentric atrophy. If destruction occurs in the internal parts, the cavity becomes much larger, even cystic, until the cortical layer may be paper-thin; this is eccentric internal atrophy. If the progressive resorption thins the trabeculae of the spongiosa, and destroys many of them, and if the Haversian canals of the compacta are made marrow-like into Haversian spaces, the process is called osteoporosis. The bones become light in weight and brittle, can be sawed like worm-eaten wood; the macerated bones are brittle.

The progressive physiological resorption is not balanced by a corresponding production; in this type of simple atrophy the number of lacunae is not increased (Pommer).

In advanced atrophy, the marrow may be composed of fluid, oily fat. Since the fat replaces the disappearing bony structure, the term "lipomasia" of the bone is used (v. Volkmann). The marrow may be lymphoid, red, or perhaps completely gelatinous.

Fibrous atrophy is the change into connective tissue, found particularly in the ends of shredded spongiosa trabeculae; it was observed by Rindfleisch and Orth, and found by Sauerborn in the bones of humans who had suffered severe chronic nutritional disturbances; extensive gelatinous change in the marrow was relatively frequent. This type is probably the cause of the increased brittleness of the bones of very old people. See also p. 1076, fig. II.

Higher degrees of brittleness are termed osteopsathyrosis. There are differentiated: a symptomatic osteopsathyrosis, occurring in diseases which reduce the rigidity and resistance of the bone, *e.g.*, simple and inflammatory osteoporosis, senile and non-senile marasmus, rickets, osteomalacia, the neurotrophic atrophy of tabes dorsalis and syringomyelia, chronic Pawlow's fistulae in animals (see Looser), permanent bile fistulae in humans (see Seidel). The infiltration of bones by tumor masses (carcinoma, sarcoma), may produce pathological fractures.

Idiopathic osteopsathyrosis (Lobstein), or essential brittleness of the bone, is a rare, often congenital, or early childhood, occasionally familial, and inheritable, etiologically quite obscure, disease, characterized chiefly by the appearance of fractures and infractions following mild insults and repeated throughout the entire life of the individual; these in conjunction with spontaneous changes in shape, lead to peculiar deformities of the skeleton (Maier). Concerning the anatomical phases of the disease, very little was known beyond a few isolated microscopical examinations (Doering; see, for example, A. Broca and Herbinet). Looser, (lit. until 1905), followed by many in his views (thus Frangenheim, lit., see also lit. by K. H. Bauer), on the basis of microscopic examinations, identifies the disease with osteogenesis imperfecta, and calls this "tarda," parallel to "congenita," and believes its cause is a diminished function of the endosteal and periosteal osteoblasts, which, however, are of normal structure. Thus bone production is insufficient and the bones become rarified without increase in normal resorption. The growth in thickness is diminished. But differentiation into tarda and congenita is superfluous and erroneous, as Sumita emphasizes. It is sufficient to speak simply of osteogenesis imperfecta. In severe cases the change may appear intrauterine, and children are born with the condition (osteogenesis imperfecta congenita), or the disease progresses without particular exacerbation for some time, and is suddenly manifested by a spontaneous fracture; the disease itself, however, should not be called tarda simply from this circumstance. Axhausen, in contrast to Looser, thinks of early osteomalacia in some cases—according to M. B. Schmidt, the malacia form of rickets—as the cause of brittleness; v. Recklinghausen believes it is impossible to include all cases of psathyrosis as examples of a single disease, such as osteogenesis imperfecta. Wieland and Niclas, Payr, share this conservative opinion, but, on the other hand, Hart, in an eleven year old boy, demonstrated the criteria of osteogenesis imperfecta (Eiken). Bolten believes a defective calcium metabolism is responsible; this is produced by a reduction in the function of the protective endocrine glands (thymus, parathyroids), and a disturbance in the sympathetic system—sympathetic hypotonia. Schabad and Hass demonstrated increase in the excretion of calcium, while the x-ray pictures of Hofmann (lit.) showed no changes that could be interpreted as rarefaction. In a case of R. Preiswerk (2 year child with osteogenesis imperfecta), the Roentgen ray picture, however, allowed the conclusion that calcium salts were present in smaller amounts and unequal distribution. K. H. Bauer (lit.), in his case, (11 year old boy), showed increased transparency to the rays, produced by a more tender interstitial growth of the trabecular system, and not by lack of calcium; see also Zesas, Kienbock concerning the so-called "light zones," which Looser believed were of traumatic origin, and explained as callus remaining without calcium for a long time; thus he called them "regressive zones." Obviously more investigations are needed. The frequent coincidence of abnormal bone brittleness with blueness of the sclera, is interesting, even though not constant; the veins shimmer through the thin covering membrane. The symptoms often appear in a number of generations; in some of the cases, progressive deafness is a third symptom.

Burrow postulates a congenital, inheritable, poor quality of the connective tissue, *i.e.*, the mesenchyme, from which the sclera and the skeleton come. K. H. Bauer (lit.), lately has spoken of a constitutional anomaly of all the derivatives of the mesenchyme, but he still believes in some of Looser's views. [For report of case and further lit. see Wagoner, G. W., Ann. Surg. 80: 115: 1924.—*Translator.*]

Types of Atrophy.—(*a*) *Senile and marantic atrophy* may occur in the entire skeleton, in varying degrees in different situations, and lead to both external and internal atrophy. The tubular bones, and particularly the spongy bodies of the vertebrae, are thus made abnormally porous, breakable, and compressible; they can be sawed like worm-eaten wood. The bones of the face and the skull are involved to particularly high degrees. The flat bones of the skull, the shoulder blades, the hip bones, may be very thin. According to Virchow, the situations on the flat bones become more atrophic, which have few muscles, or at least are free of tough tendon insertions; it may, however, occur on the skull and the upper part of the temporal bone where the contrary circumstances are present; see below, (fig. 520).

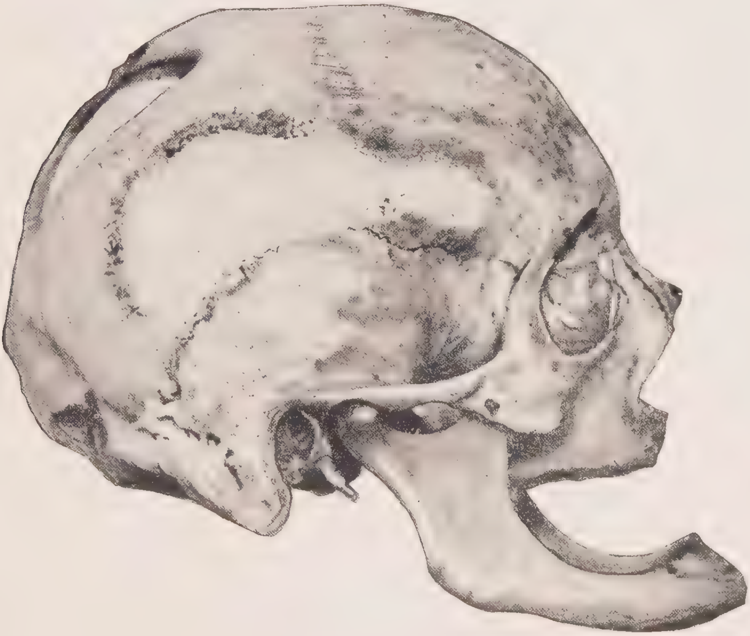


FIG. 520.—General senile atrophy of all skull bones, especially the translucent thin parietal and temporal bones; about ½ nat. size.

Particularly the vault of the skull becomes more and more thinned, rough, finely porous, and covered with deep vessel furrows, the emissary openings are dilated; the diploe at first are dark blue red, later, with increasing thinness and disappearance of the external table, they are laid bare (raw and red), and made to disappear even along with the tabula vitrea. New bone is, however, laid down in the opened marrow cavities, so that a thickening and smoothness follows in the restored parts. On the internal surface of the frontal bone there may be new formation as thorny, rough, hard thickenings, occasionally of considerable extent. Over the parietal bone there are long, deep furrows on both sides of the skull; here as well as in the posterior fossa, the bones become almost transparent and parchment-like, even perforated in focal places, so that the galea aponeurotica, the gliding of which Chiari believes is responsible for the atrophy, and the dura come into direct contact. This senile symmetrical furrowed atrophy may, as Chiari says, extend to the plana temporalia, which is important in considering the significance of muscle pull and pressure. The skull illustrated in fig. 520, shows these circumstances in an outspoken way. Chiari called attention to a sinking in of the bones of the skull along the coronary suture with disappearance of the suture teeth; the sutures between the bones were, in general, contrariwise to the ordinary conditions, *i.e.*, entirely, or almost entirely open. The atrophy in the toothless upper and lower jaw bones is very typical (fig. 520). The tubular bones and the flat bones of the breast and pelvis, are attacked by both internal and external atrophy, become smaller and less heavy; the atrophy tends to be particularly marked around the joints. When the neck of the femur is sawed open, the architecture may be seen particularly well, inasmuch as just those typical trabecular systems are retained longer, which are recognized as the most important mechanical trajectories. In rare cases, all flat bones are perforated by innumerable holes, and appear quite worm-eaten. The bodies of the vertebrae are sometimes merely porous, in other cases, relatively smaller, so that the vertebral column is shortened by a number of centimeters. If the atrophy is unequal, the result is deformity of the vertebral column (senile kyphosis, scoliosis).

According to the consistency, the senile bones are (1) those which are abnormally brittle, tough, non-bendable, in which senile osteoporosis, and thus osteopsathyrosis, brittleness, is present in the usually well calcified bony tissue; (2) those in which the actual firmness of the bony tissue is diminished, and the bones become abnormally soft, can be easily bent and cut, and in which the atrophy is caused by the appearance of osteoid seams. This is also called the senile form of osteomalacia; it shows clinically, among others, the symptom of becoming smaller, which is lacking in osteoporosis (compare the first observations, p. 1074).

According to Schlesinger, there are temporary transitions from senile osteoporosis to senile osteomalacia.

In senile atrophy, the bone marrow is frequently fatty or gelatinous; in some short and flat bones, it may retain the characters of red marrow (p. 287).

Marantic atrophy may occur in younger individuals who have suffered from chronic marasmus. It may take the form of a severe degree of general osteoporosis or osteomalacia.

The question is asked if "alimentary" spontaneous fractures, which follow undernutrition, and which are regarded as possibly late rickets, or possibly as hunger osteomalacia (see p. 1072, and also under late rickets), may be produced by an osteoporosis alone (pseudorachitic osteoporosis). Szenes believes it is possible, but in most of the cases there is a combination of both late rickets and pseudorachitic osteoporosis.

In hunger with insufficient calcium ingestion, the destruction of bone is an autolytic process (Neurath), and in all animals with nutritional bone diseases, it seems that there is chiefly an osteoporosis (Roloff, Gans, Reisinger). Schmorl found osteoporosis in dogs fed on diets poor in calcium and phosphorus; while in merely calcium deficient diets, osteoblasts are present, and produce much, but not completely calcified, new bone; in phosphorus-poor diets, the function of the osteoblasts themselves is inhibited. In calcium-poor diets, Dibbelt found osteoid seams, but then also osteoporosis. Many authors assume there are temporary transitions between osteoporosis and osteomalacia in "hunger osteopathy" (Schlesinger, Kirch; see pp. 1072 and 1160).

Osteoporosis of general distribution is also met in scrobutus or scurvy, a chronic disturbance of metabolism due to improper qualitative nutrition (Aschoff, Koch).

(*b*) **The atrophy of inactivity** is simple and quantitative, occurring most obviously in the long bones, when the use of an extremity is lost during its growth period. The bones become thin, are easily macerated and almost translucent, they are also short. It may be caused by paralysis, *e.g.*, of central origin, by poliomyelitis, or following long inactivity for other reasons, among which inflammations of the bones and the joints may be mentioned.

Inactivity atrophy may be seen in one half of the pelvis, when a leg is not used for a long length of time, also in empty bone cavities, thus in the orbit after removal of the bulb, the alveoli after removal of the tooth, the acetabulum after removal of the head of the femur, etc. Amputation stumps of hollow bones become pointed and conical (concentric atrophy, see fig. 522). The bony atrophy of gun-shot fractures of the extremities is believed to be due partly to inactivity, and partly to nutritional disturbances from ischemia (Hilgenreiner). Even after the definitive formation of bones after fracture, in some of the cases, those parts not necessary for the static position undergo atrophy, and the porous bony masses undergo a complicated change, partly destructive, and partly rearranging of their "static elementary parts" (Roux).

(*c*) **Pressure Atrophy is Very Frequent.**—The atrophy caused by increased resorption, both lacunar and smooth, occurs under the influence of continuous pressure even from a very soft and elastic substance. As example may be mentioned, the Pacchionian furrows from the pressure of the Pacchionian granulations, also the erosion of bone by aneurysms, particularly those of the aorta, with disappearance of the vertebrae, the ribs, the sternum, and not rarely perforation of these parts.

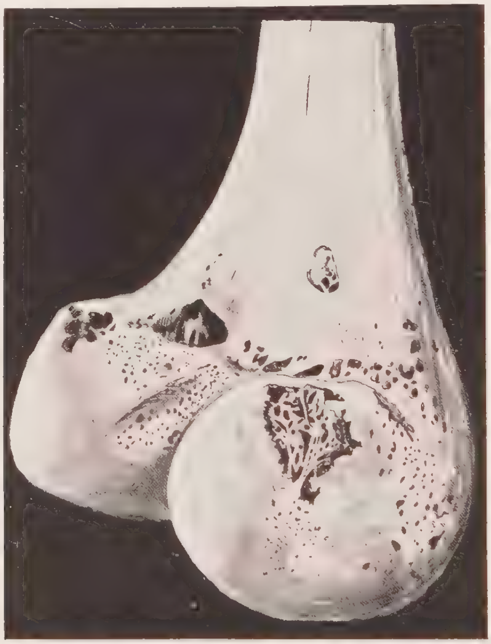


Fig. 521.—Very pronounced internal atrophy of lower epiphysis of femur, 16 years after resection of hip-joint; girl 25 years old; ⅞ nat. size.

Increased intracranial pressure from hydrocephalus or cerebral tumors or abscesses, may universally thin the skull, or produce irregular furrows on its inner surface. (The free calcium is removed partly by the lymph into the dura, lit. M. B. Schmidt.) Tumors of the dura, or hair follicle tumors of the scalp, have perforated the skull. From overstretching of the abdominal walls and the pressure of tumors, *e.g.*, an ovarian cyst, the pelvic bones become thin and porous. Pressure atrophy is also produced by tumors or inflammatory products in the rigid walls of bone cavities, *e.g.*, cholesteatoma of the middle ear, fibrous or sarcomatous, richly vascular, nasopharyngeal polyps, tumors or chronic accumulations of fluid in the antrum of Highmore, intraorbital tumors, those of the alveolar processes (tooth cysts and epuli), tumors lying against bones, such as the primary external or internal actual bone tumors, or metastatic bone tumors and parasites, (echinococci) in the internal parts of the bone.

In the neighborhood of the pressure, there is occasionally a reactive appositional new formation of bone preceded by sclerosis as an expression of mild inflammatory irritation, while the destructive process continues.

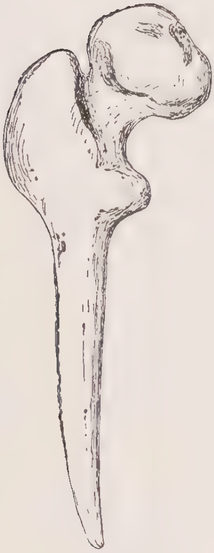


FIG. 522.

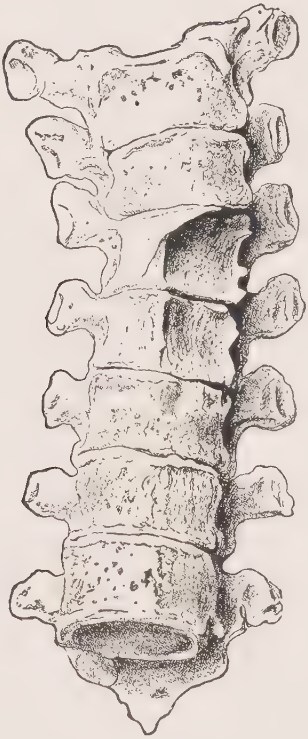


FIG. 523.

FIG. 522.—Very marked atrophy of stump of femur; conical end and increased curvature of the shaft; 10 years after amputation of femur of 29 year old tailor. Circumference below the lesser trochanter 7.6 cm. (healthy femur 10.5), all other measurements reduced correspondingly; ½ nat. size.

FIG. 523.—Pressure atrophy of several thoracic vertebrae due to an aneurysm of the arch of the aorta; scoliosis of spinal column.

In the experiments of Jores, the application of constant pressure led to disappearance by lacunar as well as smooth resorption (p. 1052); new formation appeared on removal of the pressure.

When endosteal inflammatory tissue overgrowths, or granulations, with or without suppuration, lead to progressive disappearance of bone, the condition is known as caries. Erosion is bone disappearance from pressure without inflammation.

(*d*) **Neuroparalytic and Neurotic Atrophy.** The former is a consequence of inactivity of paralyzed members, *e.g.*, in the paralysis of children. Neurotic atrophies are observed in diseases of the brain or spinal cord without paralyses, thus particularly in tabes dorsalis (in the tubular bones and also the vertebrae), and dementia paralytica, syringomyelia, etc. The bones may present the picture of an eccentric atrophy, become brittle, or abnormally bendable, and resemble those of osteomalacia. Spontaneous fractures occur very readily. Because of the obscurity of the relationship to central nervous diseases, this atrophy is termed merely neurotic.

The bones of the extremities in the paralyses of childhood may remain stationary in their length and thickness. To this class belong the changes in the bones of the face and skull following older paralyses of the facial nerves (lit. Pichler); these illustrate the relationship between weakened facial muscle function and diminished bone growth. (For other views, see Hildebrand, lit.)

The neurotic bone atrophies following nerve gun-shot wounds, without there necessarily being an injury to specific atrophic nerves (lit. Bruning), are according to Lehmann (lit.), due chiefly to reflex changes in vagotonus, which alter the blood distribution and the nutrition of the bony tissue. The spontaneous fractures in tabes occur particularly in the lower extremities, and are almost entirely painless. Consolidation is not interfered with; even hypertrophy of a callus is not rare (Baum). In syringomyelia, the bones of the upper extremities are preferred (lit. by Grunert), and it is thought there may be a trophoneurosis in the sense of Romberg. No definite trophic nerves have ever been demonstrated, however, and it is rather a functional and atrophic influence that is at work. Functional irritation increases assimilation, *i.e.*, the trophic activity, which is particularly true of muscles and glands. On the other hand, diseases, or lesions of the sympathetic vasomotor nerves, produce indirect trophic disturbances (Roux); in the bones, however, in addition to this cause, there is also an inactivity atrophy, *e.g.*, when arthropathias appear in tabes, the resulting rest position produces an osteoporosis. (For other views, see Monckeberg; compare Schubert.) (See under the chapter, neuropathic arthropathias and trophoneurotic atrophies under leprosy, p. 1147.)

The rare hemiatrophy of the face (hemiatrophia facialis or faciei progressiva) belongs to this type of change. It appears even during the period of growth, as a primary disease of the peripheral trigeminus (Virchow, Mendel, H. Curschmann), or of the sympathetic (Seligmuller, Jendrassyk, Oppenheim), or it takes on a focal, hemiatrophic form and there is coordinated with it an infectious disease of the trigeminus (Mobius); in some cases there is thought to be some sort of a relation to chronic lung diseases (lit. Weinberg, Hirsch). Stier and Boenheim class it with the hereditary degenerative diseases. Lit. by Marburg and Coenenberg.

Roentgenologically, Sudeck showed that an acute bone atrophy was quite frequent, not only after inflammations of the larger and smaller joints, but even after phlegmons of the soft parts. More rarely, it occurs after traumata. Further, according to Sudeck, inflammatory irritation exerted on the bone marrow near to the inflammatory focus, leads to atrophy, *i.e.*, a "trophoneurotic" atrophy, produced reflexly from peripheral irritation; but Monckeberg prefers to consider this form an inactivity atrophy.

A very peculiar disappearance of the bodies of the vertebrae, osteolysis, of obscure pathogenesis, has been described by Schlagenhaufer.

> **Translator's Remarks.**—According to Allison and Brooks (Surg. Gyn. & Obst. 33: 250: 1921), there is no evidence that any disease process plays a role in the production of bone atrophy other than its effects on use. Dogs, in the experiments, were subjected to section of the brachial plexus, excision of the upper end of the humerus resulting in a flail joint and plaster of Paris fixation.

True, Pure Osteomalacia

This is in contrast to senile and marantic osteomalacia, to those observed in certain psychoses, to hunger osteomalacia (see below), and to bone softening from other causes such as severe rickets, tumor infiltration, etc.

When the term osteomalacia is used, it is usually in the sense of a chronic, general disease of the skeleton, particularly frequent in certain parts of the world, such as in Lombardy, Niederrhein near Cologne, Westphalia, east Flanders, etc., and far more frequent in the female sex.

An actual immunity in certain regions, *e.g.*, the shores of the Oder (Cohnheim), probably does not occur, because in Silesia many cases of puerperal and non-puerperal osteomalacia have been seen clinically (Kroner and others), and have also come to autopsy. v. Winckel believes there are seven different causes of the disease, which may be arranged according to the time of their influence: damp climate, too little clothing, poor nutrition (potatoes, sour bread, etc.), pregnancy, with its giving up of calcium to the fetus, birth and puerperal changes—in which a protracted lactation is said to have a particular influence—hard work in the open, and finally, sorrow and disappointment. According to Kehrer, however, the disease may occur under more fortunate circumstances, to which W. Busch called attention, while speaking of a case of severe ostoemalacia which was cured by the administration of Wegner's phosphorus pills (the actual formula can be found given by Oppel).

Hunger malacia of the bones, or hunger osteomalacia, called by others hunger osteopathy, was first met in 1919 in Vienna, with explosive suddenness, produced by diminished nutrition, and spread over a large population (Edelmann); in its completed form, it is a typical osteomalacia (Schlesinger), and is favorably influenced by giving cod liver oil (0.02 phosphorus in 100 cc. of oleum Jecoris aselli, 2–3 tablespoonfuls a day) and a solution of calcium salts (calcium chloride, 2–3 grains daily). There may actually occur osteomalacia "epidemics," particularly in women (Schiff), but in men as well, usually in older individuals; Schmorl believes these cases are senile osteomalacia (see also Hecker). Schlesinger speaks of a partial hunger osteopathy, characterized by spontaneous fractures in youthful individuals, a disease first described by Fromme in Gottingen, and likewise produced probably by insufficient nutrition, but regarded by many as late rickets. The close relationship between osteomalacia and rickets (see p. 1075), has been recognized since the time of Glisson (p. 1151), and osteomalacia has often been called rickets of adults, in contrast to the rickets of childhood and adolescent years until the time of puberty (Hirsch).

The disease involves chiefly women who have frequently, and rather easily, borne numerous children (v. Winckel); in fact, those suffering from osteomalacia are said to be particularly fruitful. The disease may progress to severe degrees during pregnancy. It has also been called puerperal osteomalacia, and may be contrasted with the rheumatic form, which occasionally occurs in nullipara, as well as in men, who, however, rarely show severe degrees. Finally, it is probably justifiable to extend the idea of osteomalacia much further, and to rid ourselves of the opinion that it is chiefly a disease of pregnancy, for exclusive of cases during middle life in both sexes, there is a true senile osteomalacia (see O. O. Weber, Ribbert and others, lit., Schlesinger). This latter, by combination with severe atrophy (osteoporosis), is characterized by broad osteoid seams.

According to the investigations of v. Recklinghausen, Rehn, Siegert, Anschutz, Sauper, Axhausen, typical osteomalacia occurs in childhood; also, in fact, many cases in which changes in the contour of the skeleton are found, such as are produced otherwise by puerperal and senile osteomalacia, v. Recklinghausen would trace to an osteomalacia of childhood, *i.e.*, the malacia or severe variations of rickets. Also such deformities as genu valgum, coxa vara, etc., may be looked upon in large part from this point of view. (It is worthy of note, however, that Hecker, *e.g.*, in spite of the conditions in Dresden, which favored poor nutrition, found no increase, but actually a decrease in the rickets of children.)

This disease begins with rheumatic pains in the back, along the vertebral column and the ribs; its most remarkable change is a gradual diminution in the amount of calcium salts and a softening of the bones, most obviously of those (also clinically), which are the chief supports of the body, viz., the vertebral column, the base of the skull, bones of the pelvis, the neck of the femur. These become flexible, and in the more severe degrees, soft, so that they cut like wax (osteomalacia flexibilis sivecerea). In still severer grades of softening, the bones appear like membranous tubes filled with a soft pulpy mass. In other cases, thin layers of calcium-containing substance are retained in the cortex, making the bones fragile (osteomalacia fracturosa, fragilis) see fig. 524. In most cases, however, the brittleness and softness are not so striking.

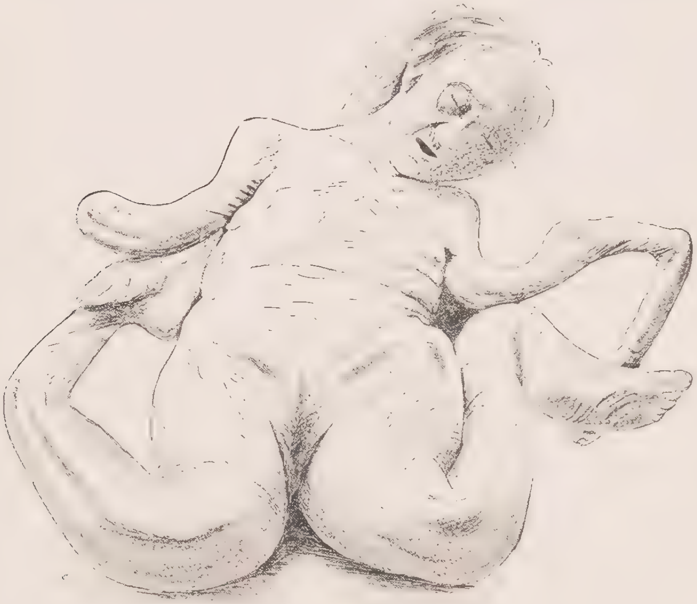
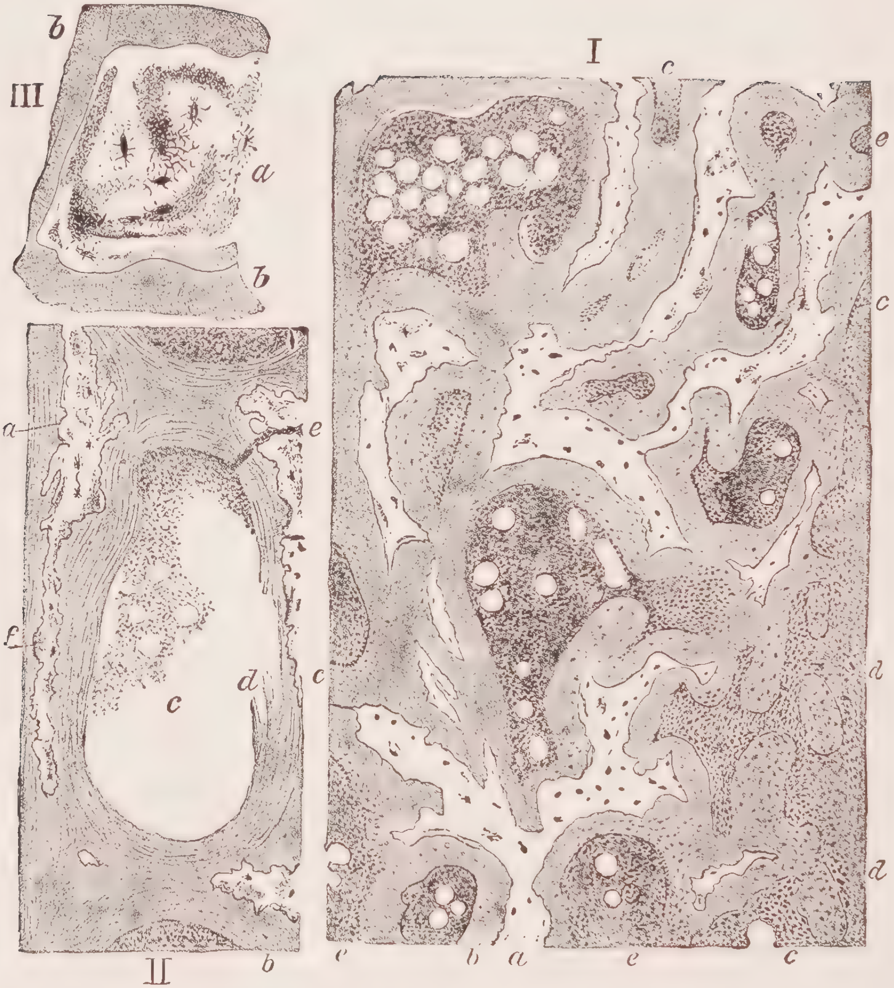


FIG. 524.—Most intense osteomalacia in a woman of 64 (from Canton Schoffhausen, Switzerland); body weight 26.23 kgs.; length 139 cms. True conjugate 8 cms.; marked calcareous deposits in both kidneys. The laryngeal skeleton was purely cartilaginous with exception of a small bony spot in the thyroid cartilage the size of a pinhead. (v. Recklinghausen, Rachitis and Osteomalacia; 1910, p. 413, hypothecates fibrous ostitis in this case.)

There is probably no such fundamental difference between osteomalacia flexibilis and osteomalacia fracturosa, as stated by Killian; both may occur together, or bones which at first are fragile, later become flexible. The elasticity is often only apparent, inasmuch as the bendable bones show numerous fractures as in fig. 524. Purely osteoporotic bones break easily, but do not bend.

The changes in true osteomalacia are characterized particularly by diminution of calcium in the skeleton, and histologically, by richness in osteoid tissue. It does not consist, however, as was formerly assumed, simply of an halisteric bone disappearance, but in many cases there is a coincident vigorous, at first calcium-less, osteoid bone formation. We thus have osteoid bone substance produced by the decalcification of old bones as well as by the formation of new uncalcified bone. Resorption processes are undoubtedly important. Thus the calcium-containing bony trabeculae of the cortex become more and more decalcified, so that their situation is finally taken over by a fibrillar (stainable with carmine) connective tissue, which then disappears, and is removed in the dilating Haversian canals and narrow spaces. We thus see both building up and destruction, but different from the physiological, inasmuch as both occur coincidently, or following each other, in improper proportions (v. Recklinghausen). This vigorous tendency to bone formation explains the surprising fact that fractures in those with osteomalacia tend to heal with luxuriant, even though poorly calcified, calluses. In senile and marantic osteomalacia, this is not the case. Here, the tendency to new growth is lacking, and a large part of the bone which seems to be decalcified, has in reality, not yet been calcified. Senile malacia bone always remains porous, and does not become tough, such as often may occur in the bony tissue of true osteomalacia. The bone formation may go so far, that large parts of the old bones are replaced by new osteoid tissue, at first calciumless, and later calcified in the center of the trabeculae, tough, and finely porous. In this case, therefore, there is complete replacement, but in other cases, in addition to the disappearance of old bone, there is a vigorous application of osteoid tissue as a finely porous, tough, sandstone-like structure (p. 1076, illus. I). This occurs particularly in the bodies of the vertebrae, but also in other situations such as the neck of the femur, the pelvis, the sternum, more rarely in the flat bones of the skull. In isolated cases, the internal thickening of the bone varies considerably in its strength; the process is often closely related to osteoporosis; in fact, this change may predominate so that we might call it enostosis. Thickening of the spines or tuberosities, to which are attached stronger muscles, tendons and ligaments, leads to such changes in the external configuration of bones that actual exostoses may be formed (v. Recklinghausen).

The resorptive processes in pure, true osteomalacia, as already stated, are characterized by the appearance of "osteomalacia" or "osteoid seams." Stripes of decalcified or non-calcium-containing bony tissue appear first on the edges of the bony trabeculae. These seams which stain densely with carmine, have a homogeneous, or, at the most, a finely striated, but occasionally a very obvious parallel fibered structure, (figs. 525 to 527), and contain but a few small bone bodies. Non-calcium-containing situations also occur in parts of the bony trabeculae. The boundary between the calcium-containing and non-calcium-containing parts of the bony trabeculae is often angular, lacunar and very irregular. In the border zone, as well as in the interior, of the calcium-containing homogeneous trabeculae, even without particular preparation of the sections, many granular and light brown areas may be seen; these are the reticulum figures of v. Recklinghausen, which as in figs. II and III, p. 1076, may be made visible by the injection of carbon dioxide, and which v. Recklinghausen believes are an expression of previous decalcification (p. 1054). These are particularly numerous in the boundary zones of non-calcium-containing and calcium-containing bones, and even internally in the still calcium-containing parts. As emphasized earlier (p. 1054), they are not found in decalcified tissue. They are, therefore, quite important in demonstrating decalcified older bones, and in establishing the idea of osteomalacia seams as decalcified bone. This is denied by Looser in spite of recent demonstrations by v. Recklinghausen; see p. 1055. In fairness it must be said that the older view of osteomalacia seams, as newly laid down, but still uncalcified tissue, has been gaining more and more adherents (Cohnheim, Pommer, Kassowitz, Schmorl, Looser, Axhausen and others); so that we would have no differentiation of osteomalacia from rickets, in which latter disease the formation of new osteoid seams is typical histologically. Morphologically, or, as Looser, M. B. Schmidt, say, "anatomically identical," does not mean that rickets and osteomalacia are fundamentally similar, particularly not in the adult (see also Zuntz, lit.). Naegeli characterizes rickets and osteomalacia as genetically and fundamentally different diseases, but having as a point in common the secondary softening of the bones. The bone corpuscles are often of irregular contour (fig. III); the ends of the bony trabeculae are fringy. The formation of Volkmann's or perforating canals is particularly vigorous (p. 1076, illus. IIe). These, and more especially, simple solution of the free edges, cause the osteoid ground substance to disappear, but Howship's lacunae and osteoclasts are quite sparse (in sharp contrast to ostitis deformans!), and perhaps even less numerous than in a normally growing bone. As decalcification and resorption of the bony trabeculae proceed, the bone spaces are increasingly dilated. The Haversian canals become wide Haversian spaces. Where the bony defects are larger, the marrow is liquefied, and the results are large or small smooth-walled cysts with water clear, or yellow contents. The decalcified tissue remains fibrous, here and there, but soon disap-



FIGS. 525-527.—Puerperal osteomalacia; woman 33 years old; 6 years sick; 4 births; Cesarian section. Section from one of the lower thoracic vertebrae. The spinal column, sternum, pelvic bones were macroscopically exceptionally dense due to the formation of osteoid tissue filling the marrow spaces. a, old bone, the calcified trabeculae (light colorless) are much reduced; b, osteoid (malacic) borders (red). The grumous, finely granular areas which are independent of the shapeless bone corpuscles are reticulum figures; c, osteoblasts; d, formation of osteoid columns with abundant irregularly placed bone corpuscles; fibre marrow. This area lies close to the periphery of the vertebra; e, marrow spaces. Hardened in Muller's fluid, carmine stain. Low power. II. Non-puerperal osteomalacia in a seamstress 37 years old with kyphosis of the spine which was soft enough to be cut with the knife. a, bone some containing calcium, many lattice figures f; b, decalcified bone; at d fringed out and torn; c, marrow space; e, perforating canal. Carmine stain, carbonic acid injection. (Low power.) III. Reticulum figures in the internal bone trabeculae, most still-containing calcium; a, large shapeless bone corpuscles; b, fringed and combed striated decalcified bone substance; detail from II. Carmine stain, carbonic acid injection. (High power.)

pears, probably with the richly vascular marrow tissue. Then there remain merely isolated decalcified trabeculae in a fibrous, richly vascular, ground substance.

New bone formation in osteomalacia consists of osteoid, *i.e.*, non-calcium containing substance laid down by osteoblasts, sometimes to considerable extent, so that the spongy structure becomes denser and finely porous. The new tissue may extend to parts of the intervertebral discs. According to v. Recklinghausen, this osteoid appears chiefly where the pressure and pull are most marked, thus on spines and tuberosities, to which stronger muscles, tendons and ligaments are attached, and on points of bending and situations of fracture. The osteoblasts, accumulate on preexisting trabeculae, and in the fibrous medulla on the situations named, which are then covered with the many osteoid-containing, evenly distributed, plump, large, bony bodies with few outrunners. In situations of marked mechanical deformity (bent neck of the femur, vertebrae), the ground substance is woven, non-lamellar, and encloses Sharpey's fibers. It changes into bone by taking up calcium salts, first in the central parts, which still show osteoid seams (Ribbert); the latter author believes new bone formation is so important in osteomalacia, that seemingly unchanged or even rarified parts, contain actual thickened isolated bony trabeculae, and real changes in their architecture. v. Recklinghausen considers Sharpey's fibers (p. 1056), in situations where they otherwise do not occur, as important in demonstrating the neoplastic nature of this osteoid tissue. The formation of osteoid—malacia—tissue, is another point of similarity to rickets, and a point of contact with ostitis fibrosa, *i.e.*, metaplastic malacia.

The marrow becomes fibrous or fibrillar in these finely porous situations where there is much osteoid; in general, the fatty marrow is changed to lymphoid, which has a hyperemic dark red to brown red color; then the bones can usually be cut with a knife. Hemorrhages and pigment cells also appear in the marrow. In other situations the marrow remains yellow or becomes gelatinous. See Naegeli, concerning hyperplasia of the marrow and secondary blood changes.

Puerperal osteomalacia begins almost always in the pelvis, and is accompanied by piercing, boring pains. It is occasionally localized to this situation and the neighboring parts of the trunk (at least macroscopically). The non-puerperal form begins in the vertebral column and the thorax, less often in the skull, and if diffuse, is usually more severe than the puerperal type. Osteomalacia is, as a rule, progressive. If it heals with calcification and bony change of the osteoid, the bone may become sclerotic as in rickets.

Disturbances of motility, such as pareses, paralyses, muscle contractures, tremors, etc., appearing even in the beginning, are perhaps of central origin (Pommer, v. Hosslin). Pineles thinks of a functional change in the parathyroids, but according to Siemerling, the paralyses are due to fatty changes in the musculature, particularly of the legs.

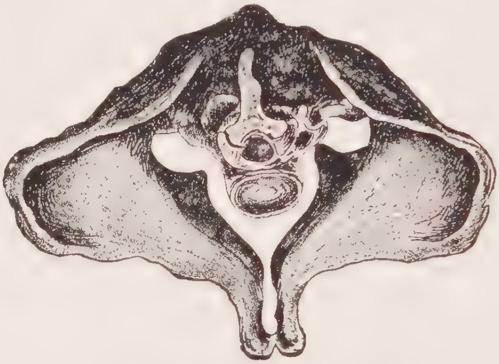


Fig. 528.—Osteomalacia pelvis, viewed from above.

Among the changes in the skeleton which are due to its softness, those in the pelvis are the most important, and the most typical. The pressure of the trunk on the sacrum, and the lateral pressure of the healthy heads of the femurs produce a heart-shaped or three-cornered, or clover leaf contour, to the pelvic aperture (figs. 528 and 529), while the pubic bone becomes beak-shaped. The pelvis is small, light in weight; the bones are thin, bendable, occasionally brittle; they are often yellow or dark brown, and feel fatty.

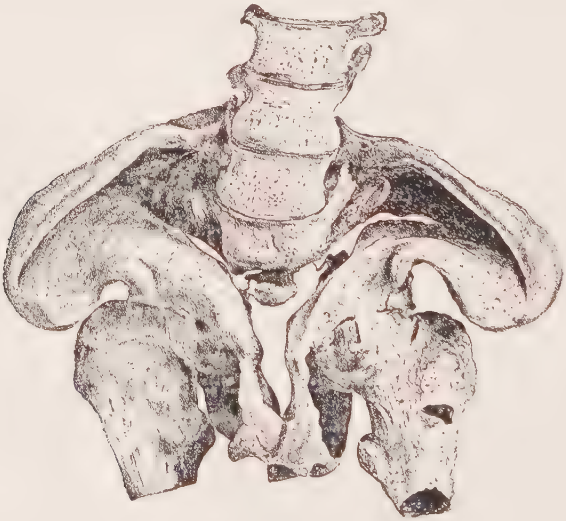


Fig. 529.—Extreme osteomalacia of pelvis. (Published by Gelpke; Osteomalacia in Ergolztale, Liestal, Switzerland, 1891.)

These changes in the pelvis are not as typical in senile osteomalacia as in the puerperal type.

The vertebral column may show various kinds of deformities such as kyphosis, lordosis, scoliosis (bending toward the posterior, forward, toward the side). The intervertebral discs may ossify, and produce synostoses of the vertebrae. The vault of the skull may be bendable, very light in weight, porous or dense; the base of the skull shows elevations (kyphosis). The ribs are frequently pushed inward, particularly in the anterior axillary line, and often kinked. We see healed fractures in which the callus remains osteoid and still contains cartilage. The sternum may be pushed forward, or angulated. The longer tubular bones are usually not involved, or in only their spongy portions, and rarely to high degree; when they are, they show porous enostoses, kinks, bendings, and breaks. In very rare cases, almost all the bones may participate and the entire body is changed into a deformed mass of flesh (fig. 524 p. 1076).

The actual cause of osteomalacia is still doubtful, even though the general causes have been well studied (p. 1072). It was formerly assumed that too much lactic acid was produced in the digestive changes, both in the intestinal canal and in the bones; this, in conjunction with a low calcium diet leads to decalcification (acid theory); but many objections to this view can be raised, *e.g.*, an acid reaction of the blood must necessarily lead to precipitation in the blood itself (Hoppe-Seyler). Another view states that an active process is present, closely related to ostitis and osteomyelitis, and perhaps only a special form of these (v. Volkmann, Basset and others). v. Recklinghausen assumes there is congestion, actual arterial hyperemia of the bone marrow, caused by local irritation of the vascular bone apparatus especially since the bones usually involved are those in which mechanical difficulties might occur; following this arterial hyperemia, physiological repair and destruction occur simultaneously or following each other but in excess; the marked destruction is produced because an increased amount of fluid passes through the bones, takes up the interstitial substance, and then the bone fibers themselves. Naegeli believes it more probable that the bone marrow is the chief factor concerned. The healing after removal of the ovaries, first described by Fehling, is thought to act favorably on these circulatory conditions. Even earlier, vaso motor influences were supposed to be important; on the basis of his results following castration, Fehling advanced the hypothesis that irritation of the vaso dilators of the bone vessels was brought about reflexly from the ovaries, produced hyperemia of the marrow, and by increased resorption, hastened halisteresis. The treatment of osteomalacia with adrenal substance, as recommended by Bossi, has its basis in the belief that this produces vaso constriction. Older anatomic investigations of the ovary were quite negative (Bulius, Sonntag, Goth); Wallart described marked development of the so-called interstitial ovarian glands in gravid and non-gravid osteomalacia patients (see also Kaji, Falk), so that some sort of a relationship between osteomalacia and the internal secretion of the ovaries was postulated; now, however, the importance of the so-called interstitial ovarian gland is doubtful, and the finding of healthy, well developed, so-called interstitial glandular tissue after x-ray castration (Wallart), which has a beneficial influence on osteomalacia, speaks against their importance in the genesis of osteomalacia. Perhaps it is better to think of other parts of the ovary, particularly the corpus luteum; thus there is the view, that hyperfunction of the ovary is important, and that this directly and through influences on other organs of internal secretion, leads to an increase in excretion and a disturbance of assimilation of calcium (see the work from Veit's clinic; also Christofoletti, Zuntz). On this hypothesis is based the medication with hypophyseal preparations (Klotz, Weiss), inasmuch as it is believed that they are antagonistic to the ovarian secretion (Sellheim). But this theory will not hold true of the senile forms of the disease with functionless ovaries (H. Curschmann); v. der Scheer, for this and other reasons, doubts entirely the possibility of ovarian influence. The undoubted influence of pregnancy was thought demonstrated by Hanau (confirmed by Wild), when he found changes similar to those in progressive osteomalacia in the gravid or puerperal bones, but of course very mild and only demonstrable microscopically, particularly in the pelvis. (See v. Recklinghausen's critique of this so-called physiological pregnancy osteomalacia.) But Niekau, who confined these investigations to the sixth rib, saw no physiological osteomalacia in pregnant women. Grosser-Jachimovicz, (under the direction of M. B. Schmidt), confirmed Hanau's findings, but believes that the degree of this destructive process is physiological; pathological conditions are represented by diminished calcification of the newly formed bone, which allies the condition to rickets. Birch-Hirschfeld lays so much stress upon this factor, that he expresses it this way, "at least the osteomalacia of the pregnant woman is merely an excessive increase of the bone changes which so frequently take place during pregnancy," and which, as a rule, disappear after the puerperium.

Experimentally, Dibbelt produced osteomalacia in pregnant dogs by feeding them calcium-poor diets and giving them certain "calcium robbing" salts, whereby the mother loses calcium by halisteresis, although the skeleton of the fetus is sufficiently supplied. (The older investigations of H. Stilling and v. Mering were confined to merely one pregnant dog.) Concerning the poor nutritional conditions since the year 1919, and the frequently observed bone changes called by many hunger osteomalacia, see p. 1071 and literature. In extensive experiments with osteomalacia and rickets in rats, Morpurgo succeeded in growing a diplostreptococcus from the bone marrow, spinal cord and other organs; by injecting them into other animals, he produced changes similar to osteomalacia in older animals and changes similar to rickets in younger animals. Moussu and Charrin claim they have reproduced typical osteomalacia in steers, pigs, and rabbits, by injecting bone marrow emulsion from animals having osteomalacia (pigs, horses, cows, steers). Older reports of bacteriological findings in the osteomalacia of humans have not been confirmed (Lohlein); on the other hand, Morpurgo succeeded in isolating a diplococcus from various organs of a woman having osteomalacia, which, on injection into white and gray rats, produced either rickets or osteomalacia according to the age of the animal. Looser also believes in an infectious origin (and of rickets), and calls attention to the data of Ogata who described an epidemic of rickets and of osteomalacia which attacked individuals of all ages.

The alleged relationship to disease of the thyroid (Hoennicke) has not been confirmed. Scipiades reports that total extirpation of the thymus in young dogs produced an osteomalacia analogous to that of humans. The statement of Erdheim (see also Todyo, Strada, Bauer), concerning the tendency of the parathyroid to hyperplasia (p. 540), is worthy of note; it is said to be a consequence, but not the cause, of osteomalacia; perhaps it is a compensatory process to neutralize toxins produced in the ovary or other organs which increase the excretion of calcium. While an increased metabolism of calcium is necessary to provide the mineral for the skeleton of the fetus, it is increased only within physiological boundaries, but in puerperal osteomalacia it is increased pathologically; then the hyperplasia of the parathyroids is said to oppose this activity. Strata carries the argument one step further when he believes that if the parathyroids are unable to undergo this hyperplasia, tetany may appear as a symptom of parathyroid insufficiency. Cases of osteomalacia with tetany do occur. [For osteomalacia among animals see White, Corson E. P., Arch. Int. Med. 30: 620: 1922.—*Translator.*]

Regenerative and Hypertrophic New Bone Formation. Healing of Fractures

The formation of new bone, the histological details of which have been described on p. 1057 and forward, may be brought about by various causes, and appear in many forms. In one case, it is reparatory as in the healing of fractures, or causing union of surgical bone wounds, as in resections, or in the replacement of defects produced by trauma, etc., or in pathological bone changes of various kinds.

See Bier, B. Martin, concerning regeneration of the tubular bones and the importance of the endosteum (the true center of regeneration); the periosteum produces only irregular formless callus which is partly resorbed.

Osteoplastic. Teaching of bone replacement has gone through many vicissitudes. The older views of Ollier stated that living bone with periosteum of the same species, will heal with retention of its vitality; until recently, it was taught that transplanted and replanted particles of bone, living or dead, used to replace defects, do not heal, but are destroyed under all circumstances (Barth, Marchand and others, lit. by Askanazy). The implanted bone dies, and disappears without much lacunar resorption; its cells become unstainable and are removed, leaving empty bone spaces; meanwhile, it is being substituted by new bone, laid down by osteoblasts from ossifiable living tissue of the neighborhood; there is, therefore, "a slow replacement of the dead material by living" (Barth; Marchand, Enderlen), making use, perhaps, of the calcium salts of the dead bone for the construction of the new (Marchand). Wolff and David, however, adhered to the idea of living healing. Axhausen later demonstrated, in contrast to Barth's view, that in a transplanted fresh bone, the periosteum remains living, and is the chief instrument in the formation of new bone; and, secondly, that the parts in the neighborhood capable of producing bone begin to function (*i.e.*, the slumbering, but awakened by transplantation, osteogenetic ability of the connective tissue to which Macewen, Petrow, lit., ascribe the largest part of the regenerative work); but the transplanted bony tissue itself is destroyed. L. Meyer and Wehner are of the opinion, however, that some of the bone cells remain living, even though no new bone can arise from them. According to Axhausen, replacement of the dead bone occurs by successive lacunar resorption and apposition; but L. Meyer and Wehner again call attention to a "sneaky" replacement (see above). This view which partly revives Ollier's ideas (Troell believes that the entire transplant even under difficulties may remain living), found confirmation by Barth, Lawen, Lobenhofer, Lexer; but see Saltykow, Kausch, (lit.) Murphy, v. Schlotheim, (lit.), Guleke. As for transplanted dead bone, it is a foreign body; it becomes encapsulated or absorbed, or if the neighboring tissue is osteogenic, is substituted slowly by new bone.

Under other, generally varied conditions, the new formation of bone is an hypertrophy; this is seldom idiopathic, but is seen, *e.g.*, in gigantism, or in acromegaly. Usually it is secondary to many different inflammatory diseases of the bones themselves, the surrounding soft parts, or neighboring joints. These things will be discussed again after the most important bone diseases have been covered. The formation of new bone may also accompany tumors situated in the marrow or the periosteum. In other cases, it is produced by venous stasis; to this type belong the drum-stick fingers of youthful cyanotic cardiac patients, those with bronchiectasis, and others (p. 1115). Helferich, following the idea of Dumreicher and

Nicoladoni, used venous stasis in hastening the healing of fractures, by placing an Esmarch bandage about a limb; see also Bum, lit. Phosphorus and arsenic as well as other toxic substances (p. 1115) increase the growth of bone. Trauma also plays a role in hyperostoses.

When a bone becomes more voluminous by the production of new bone tissue, the condition is called hyperostosis. An abnormal increase in length of a bone is called elongation. The apposition of new tissue to the old trabeculae, or the formation of new bone trabeculae leads to a condensation called osteosclerosis, the direct opposite of osteoporosis. Very frequently a bone is both sclerotic and hyperostotic. In addition to a sclerotic hyperostosis there is a spongy hyperostosis sometimes seen, *e.g.*, in the tibia of syphilitics (fig. 1021). An enostosis is the formation of new circumscribed bony masses in the inner parts of the bones, usually in the spongiosa. An external thickening, diffusely spread, is called periostosis. Circumscribed, flat, smaller inflammatory bone overgrowths coming from the periosteum are called osteophytes (p. 1092).

Exostoses are larger, circumscribed new growths of bony tissue (hyperostoses) which appear somewhat like tumors. Many exostoses are difficult to distinguish from true tumors; these will be discussed with bone tumors (p. 1198).

The Healing of Fractures.—If a bone is broken or cracked (incomplete fracture, green stick fracture, see fig. III, p.1085), the latter is most frequent in abnormally soft bones (osteomalacia, rickets),—or if it is broken completely through, both the periosteum and the marrow are torn as a rule, and there is hemorrhage into the marrow, and neighboring tissues. (Fat embolism, p. 386, may occur in injuries to the bone marrow.) Neighboring soft parts may also be torn and infiltrated with blood.

The hemorrhage is later removed by absorption; according to some (Hildebrand), it is of no importance in the healing of fractures; according to others, it keeps the fractured parts from uniting and thus hinders healing; according to still others, (Bier, Pochhammer, Vogel), it is very important as an irritant for the formation of callus (from the fibrin), as well as being a good source of supply for nutrition (particularly in the healing of defects, see Bier, B. Martin). Within two days after a fracture, cells begin to transport the blood and tissue debris.

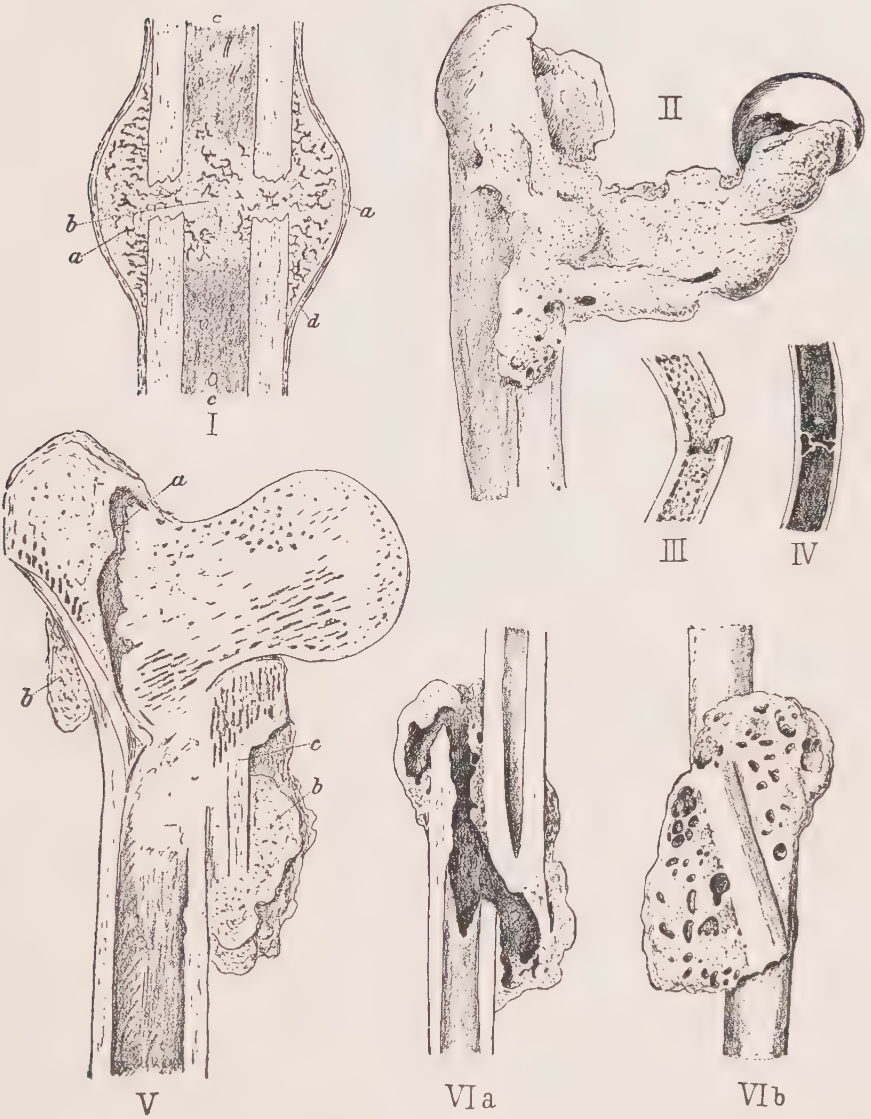
Fissures are lines and spaces particularly frequent, and often numerous in the skull, where they occur as radiations from sites of fracture especially in the lamina vitrea which is less resistant to pull; but they may be independent. The edges remain in their old positions, lie close together, and merely a fine line indicates solution of continuity. The periosteum may be completely preserved. In penetrating or comminuted fractures of the skull, the lines of separation run backward upon themselves so that a piece of bone is loosened from its surroundings and numerous pieces may be separated from each other. Another form of fracture occurs when a sharply outlined piece of bone with smooth walls, or with minor degrees of splintering of the edges, is separated from the remainder. In the skulls of new-born children, fissure fractures are quite frequently combined with funnel or spoon-shaped depressions of the bone; these occur usually from the pressure of the promontory of a narrow pelvis, and may not be accompanied by fractures.

The signs of inflammation consisting of hyperemia, exudation and cellular infiltration appear very shortly after the injury in the periosteum and in the marrow near the site of fracture. If the latter is not complicated by marked destruction of tissue or by infection, this vigorous inflammatory change disappears in a few days, and regenerative tissue growth begins from the periosteum and bone marrow; this produces the callus which unites the fragments.

This is called traumatic or regenerative inflammation, and does not extend beyond the region of traumatic irritation (F. Busch, Bruns).

The tissue from the periosteum is called external callus, that from the marrow is called internal callus.

The formation of the external or periosteal callus begins twenty-four hours after injury; indirect cell division occurs in the cells of the cambium layer of the periosteum, and in the endothelial cells of the blood vessels (Krafft); in a few days a rich granulation tissue comes from the vessels and the neighborhood. To less degree, the external layers of the periosteum and the connective tissue of the neighborhood undergo growth. At the end of the first week trabeculae and foci of osteoid or chondroid appear in this germinal tissue (fig. III, p. 1060), which is changed later to porous bone. Some of this germinal tissue takes over the situation of the marrow. The tissue from the periosteum surrounds the fragments like a spindle-shaped capsule or shell or sheet, and even extends far beyond the fracture or the periosteal or external callus (fig. I, p. 1085). In the beginning, therefore, the callus consists of germinal tissue. Then the inner layers begin to swell, the callus becomes more and more osteoid, and of gelatinous appearance; some becomes true cartilage. When the fragments can easily be rubbed against each other (Kapsammer), there is more cartilage formed near the situation of fracture; this statement is confirmed in experiments in dogs, rabbits (Giani), frogs and salamanders (Ulmann), and also in fractures of children (Kassowitz), and adults, *e.g.*, fractures of the ribs, even in very old individuals. This influence of rubbing and pressure of the ends against each other is quite evident in the origin of cartilage in both the external and internal callus. According to Gumbel, change of cartilage into bone occurs from metaplasia, and not according to the method of



FIGS. 530–536.—I. Callus formation in fracture 14 days old; fracture ends somewhat separated. a, periosteal; b, myelogenous callus, connected by the intermediary which reaches into the bone marrow c; d, periosteum. Bone trabeculae in the callus. II. Shapeless parosteal callus formation following an old pseudoarthrotic healed fracture of left neck of femur, posterior view; about ½ nat. size. III. Partial fracture of ulna; the bone is fractured on one side and kinked on the other. IV. Fracture of rabbit bone, 24 weeks old; healed without external deformity; the inner callus is also absorbed with the exception of a few delicate bone columns. V. Intertrochanteric fracture, incompletely consolidated, extracapsular; 2½ months old, with impaction of the neck into the trochanter (gomphosis); woman 80 years old. a, inner callus, soft, glassy; b, outer callus, bone finely porous; c, fragment of shaft above showing new formed supporting columns attached by finely porous callus. VI. Comminuted fracture of r. femur with marked formation of callus. VI. a. Frontal section of anterior half, view from behind the marrow cavity of the upper portion of fracture is closed. VI. b. Anterior aspect; a large separated piece of the cortical part is fixed by callus.

endochondral bone formation, because it is poorly vascular. The importance of movement is illustrated by the excess cartilage around fractures even to producing pseudarthroses (Virchow). Concerning rubbing and irritation as a functional trophic irritation in the origin of cartilaginous tissue, see also Pommer. According to Hanau and Koller, even the periosteal connective tissue preformed bone may produce cartilaginous callus, which it never does physiologically; this may be observed in such situations as the zygomatic arch where the fracture is subjected to continuous pressure and displacement by the masseter muscle. Later, the cartilage becomes bone or marrow, *i.e.*, is substituted by the invading marrow. Then the absorption of calcium changes the osteoid to bony callus; the inner layers are first to undergo calcification in the form of small white needles and streaks in the osteoid trabeculae. The external callus can be palpated externally in from ten to fourteen days. Its formation takes about thirty days. (Experiments concerning the formation of new bone after injection or transplantation of periosteum emulsion, by Jokoi.)

The formation of the internal or myelogenous (endosteal) callus begins in about twenty-four hours, with hyperemia and lymphoid change in the marrow (fig. IV, p. 1060). Osteoblasts group themselves into trabeculae, and osteoid tissue is formed from which calcified bone is made. Islands of cartilage may also appear, particularly when the fractured ends are extensively separated; the possibility of the carrying in of bits of periosteum must therefore be remembered.

Most of these cartilaginous islands later become marrow cavities. Part of the callus may be fibrous, and then be ossified. This myelogenous, or internal, or marrow callus is of minor importance in comparison to the periosteal callus. (Shown by x-ray pictures; see von Schlotheim.) Often it is but poorly developed, occasionally but a short solid tab which remains quite near to the fracture ends in the marrow cavity. (See the experiments concerning transplantation of marrow by Miyauchi.)

The Intermediate Callus. If the ends of the bones are widely separated an intermediate callus is formed between them, in which the external and internal calluses become fused. It is probably chiefly a product of the periosteal germinal tissue.

A parosteal callus appears when the connective tissue, especially the intermuscular part, participates in the healing (fig. II, on p. 1085); it may produce cartilage, osteoid tissue and bone, the latter even without osteoblasts, *i.e.*, by metaplasia (Orth). But Takata believes there is migration of periosteal cells, which become chondro- or osteoblasts (denied by Tsunoda), and Pochhammer states that osteoblasts alone are the producers of cartilage and bony trabeculae. (See Sudeck.)

(Lit. concerning callus in the appendix.)

Further Changes (Regression) of the Ossifying Callus.—The callus continues to enlarge for four to five weeks after fracture, and in seven to nine weeks is totally ossified and consolidated. Then the early, richly vascular, tender, porous, bony tissue is gradually replaced by new bone of more tough structure, as lacunar resorption and marrow cavity formation proceed, and as lamellae or new trabeculae are deposited by osteoblasts. Thus a firmer and tougher tissue is formed. This was previously called a definitive callus in contradistinction to the porous variety, but it is still not permanent, for in the course of months, or even years, especially if there has been marked dislocation or splintering, the callus itself "regresses" with rearrangement of its parts as well as of the old fractured ends.

By this transformation, the bone is reduced in size, which is useful for its function, and some of the callus is removed by lacunar resorption and the formation of perforating canals. On the other hand, situations exposed to more pull and pressure are covered by newer bony substance and the formation of statically needed denser trabeculae continues over a long period of time. The lines which run through the spongiosa are called pull and pressure trajectories. Thus there is a complete functional adaptation, (but this does not mean that the shape of the bone is necessarily restored). The resumption of function stimulates this transformation (Walkoff, Zondek, Budinger).

Even while the callus is being formed there is resorption of a number of loose or angular bony trabeculae at the situation of fracture. Later, when complete consolidation has occurred, the callus itself is materially reduced in size. If a fresh, well consolidated fracture of a tubular bone is examined, there is found externally a spindle-shaped thickening, and internally, a dense mass of bone filling out the marrow cavity. The external thickening is gradually reduced—concentric atrophy—and if the ends of the bone were approximated without dislocation, the bone, in time (years), may again resume its early form. Even the internal callus in well set fractures may be completely, though slowly, resorbed, and the marrow cavity is entirely replaced. When dislocation occurs, it usually remains permanently closed. But when the ends of the fracture are dislocated longitudinally, the old marrow cavity of both fragments may perhaps be reunited by eccentric atrophy and disappearance of the edge. In general, the definitive shape of a healed fracture, which often enough shows a deformity, depends chiefly upon the kind of fracture, *i.e.*, upon the mass of the callus.

The size of the callus varies; if regeneration is favored, the callus (chiefly periosteal), is, in general, proportional to the severity of the fracture and the degree of dislocation. In incomplete fractures—infractures, impressions, fissures, etc.,—as well as in complete, but simple, transverse or oblique fractures, without dislocation, the callus is small. It is smallest when the periosteum itself has not been torn. In the short spongy, and the flat bones, the callus, *i.e.*, the external, is also of minor quantity; the overgrowth of the marrow tissue predominates. The same is true of bone wounds; if, *e.g.*, a piece of the corticalis or the external table of the skull is knocked off (aposceparnism), granulation tissue grows upward from the open marrow cavities and Haversian canals, and this later becomes bone. (An actual callus does not develop in the skull.) In the long bones, the production of callus in diaphyseal fractures is much more marked than in fractures near to the epiphyseal ends. In comminuted fractures with splintering and marked dislocation, the amount of callus is often very large; the parosteal and the intermuscular connective tissues take part in its production as stated on p. 1086.

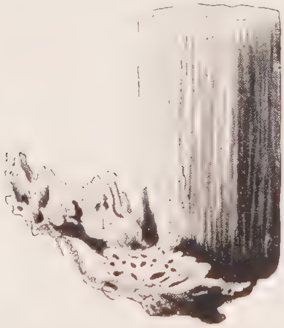


FIG. 537.—Pronged exostosis on the amputation stump of r. femur; ½ nat. size.

Experimentally, it has been shown that thyroidectomy (p. 528) hinders the formation of callus, or, at least, delays it, while the administration of thyroid extract preparations increases the rate of healing of fractures in normal animals (Eug. Bircher, lit.). After extirpation of the parathyroid glands (p. 540), there is marked delay in the formation and a diminution in the amount of callus; Erdheim found the callus particularly poor in calcium, and believes the important factor is delay in calcification.

A deformed external or parosteal callus overgrowth which does not become absorbed, is called callus luxurians, or if circumscribed, and thus similar to an actual bone tumor, is called osteoma fracturae (fig. II, p. 1085). Occasionally the bony masses spread out into the surrounding muscles and tendons in angular (fig. 537), thorn-like or shovel-shaped masses, so that the condition resembles myositis ossificans (Lange). Cartilaginous outgrowths have also been observed, and have been called chondromas or enchondroma fracturae. A luxuriant callus may be absorbed in part, or produce changes in the statics of the bones; sometimes it encloses small fragments and thus, in spite of a pseudo-arthrosis, may allow a member to bear weight, *e.g.*, in non-consolidated, extracapsular,—impacted—fractures of the neck of the femur. Occasionally, however, even an unimportant luxuriant callus so disturbs the function of a joint or muscle that its operative removal is necessary. Callus cysts also occur (Frangenheim, lit.).

If two neighboring bones are fractured they may unite in a so-called synostosis, *e.g.*, between the tibia and the fibula.

In the neighborhood of joints, all the surrounding tissues (ligaments, synovial membranes, tendons) may occasionally produce bone, resulting in ossifying bridges, and stiffening of the joints (fracture ankylosis); or neighboring bones disappear from synostosis, *e.g.*, some of the ankle bones after fracture of the lower end of the tibia and fibula.

The Time of Complete Consolidation.—In simple fractures, the rate of healing is much more rapid in children than in adults, and is almost complete in two to three weeks. In old age, and in severe cachexia, healing is delayed; in cachectic individuals, the callus frequently remains soft for many weeks. Sixty days is the average time for consolidation of a simple fracture into the diaphysis. It depends, in general, upon the size of the bone. According to Gurlt, a phalanx heals in two weeks; metacarpals, metatarsals and ribs in three weeks; clavicles in four; forearm in five; humerus and fibula in six; neck of the humerus and the tibia in seven; both bones of the lower leg in eight; femur in ten; neck of the femur in twelve weeks.

Complicated fractures with splintering, freeing of particles which undergo necrosis, extensive crushing of the soft parts, perforating skin wounds, etc., are slow to heal. Infection readily occurs, and infectious periostitis and osteomyelitis may delay the healing process for some time. Granulation tissue may appear with carious destruction of bone and with suppuration; or larger, insufficiently nourished, pieces of bone become necrotic. Concerning the healing of gun-shot wounds of the bones which represent complicated fractures, see the histological details by Walkoff.

Healing with the Formation of a Pseudarthrosis.—If bony union does not take place between the fracture ends, a pseudarthrosis results.

There may be differentiated (Brun): a pseudarthrosis in which the false joint ends may be moved, and a pseudarthrosis with more or less diastasis between the bony ends.

This insufficient formation of callus is observed when the periosteum has been removed, or in open fractures where it has been destroyed by suppuration, and has lost its ossifying ability; it occurs also when the ends ride upon each other (continuous rubbing is sufficient, according to Cornil and Coudray), or when the parts are pulled apart by muscles, as in transverse fractures of the patella, sprain fractures of the olecranon, etc.; furthermore, the interposition of neighboring soft parts such as fascia or parts of muscle hinders union; it is also hindered by rarefying ostitis, severe cachexias, and senile marasmus.

In pseudarthroses, the fragments are joined by connective tissue between the ends of the bone like a tendon, or perhaps there is no attempt whatever at union, so that the ends become hard and polished like a joint (nearthrosis). In rare cases, the ends acquire a cartilaginous covering

(p. 1086), and a capsule, which may even contain a kind of synovial fluid, but endothelial cells which characterize true synovial membranes, have never been found.

See Pommer, Schmerz, concerning the structure of the joints in pathological and artificial nearthroses.

As a rule there is no union, or, at least, union only from ligamentous structures in intracapsular fractures, particularly in older people, of which a typical example is fracture of the neck of the femur, because the loose head hanging from the ligamentum teres, which in adults contains no blood vessels (Lang), is very poorly nourished. The fractured head may disappear entirely, almost like a foreign body. In fractures of the head of the humerus the nutrition is still more meager. Healing in intracapsular fractures is better when the fracture reaches but a short distance into the extracapsular region, but it may then lead to marked callus formation and consolidations.

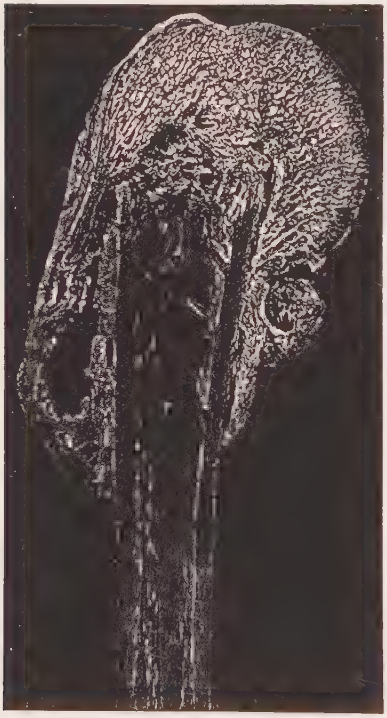


FIG. 538.—Impacted fracture of r. humerus fixed by immense callus. The diaphysis is wedged into the head (gomphosis); man 67; ½ nat. size.

Occasionally, however, particularly of the neck of the femur, there is union because one of the fractured ends is forced into the spongy mass of the other (gomphosis), or because one of the ends is well nourished and vigorously growing, so that its callus surrounds and fixes the other end (fig. 538). This extracapsular callus may, *e.g.*, bridge over the hip joint.

Changes in Form Following Dislocation of the Fragments.—The fractured ends are frequently dislocated in various ways and in different combinations.

1. **Dislocatio ad axin;** the fracture ends are approximated but their long axes form an angle with each other. The member appears as though kinked or bowed.

2. **Dislocatio ad latus;** the ends are lateral in their direction to the oblique axis of the bone, but may still partially touch each other.

3. **Dislocatio ad longitudinem;** the fragments are displaced in the direction of the long axis, along side of each other (fig. VIa and b, p. 1085),

over, or behind each other, or are pulled apart; the first is more frequent and leads to shortening; the latter is rare and leads to elongation, *i.e.*, to a diastasis. The fragments pushed past each other may touch, lie upon each other, or be completely separated. A space is left particularly frequently, where vigorous muscles are inserted on the torn particles, such as on the olecranon and the patella.

A particular form of dislocatio ad longitudinem is the above mentioned wedging of the fragments (impaction, gomphosis), which is most frequent in extracapsular fractures in the neighborhood of the trochanters, or the neck of the femur (fig. V, p. 1075); the neck is forced into the trochanter, sometimes so tightly that the clinical diagnosis of fracture is difficult, since neither abnormal mobility nor crepitation, the two cardinal symptoms of fracture, can be elicited.

4. **Dislocatio ad peripheriam;** the one fractured end, always the lower, is turned in its long axis; the upper remains in its old position. The ends no longer fit accurately. [For discussion of bone repair and good illustrations see Bancroft F. W., Arch. Surg., 5: 646: 1922.—*Translator.*]

Inflammations of the Bones and Their Results

According to the situation of the process, *i.e.*, periosteum, bone marrow, or bony tissue itself, we speak of periostitis, osteomyelitis and ostitis. Ostitis, however, does not mean an inflammation of the actual bony substance; it is rather a particular form of osteomyelitis, in which the inflammation arises first in the vascular canals of the spongiosa and compacta; the marrow tissue which lies in the canals then becomes involved, and this leads to secondary changes in the surrounding bone.

According to the clinical point of view, acute and chronic inflammations may be differentiated, or an anatomical classification may be adopted. We will first discuss the individual anatomic forms of inflammation.

Periostitis. Periostitis Fibrosa.—Under the influence of chronic, long lasting (years) irritation, there appears a tough, scar-like periosteal thickening tightly adherent to the bone. The most important part in the formation of the connective tissue is taken by the external layer of the periosteum.

This form occurs in the elephantiasis cruris of chronic leg ulcers, in which the subcutaneous tissue becomes scarred and thickened (fig. 95), in older necroses in the neighborhood of chronic inflammatory arthridites, etc. Traumas such as contusions, pressure, etc. may produce a cicumscribed cicatricial thickening of the periosteum, which develops as a soft, painful, voluminous, exudative swelling. According to Ponfick, small bacterial foci in the periosteum in various infectious diseases may also lead to thickening, tight adherence of the periosteum, and superficial rarefaction of the bone.

Periostitis Ossificans.—In this form, the inner layer of the periosteum produces bone. This newly built tissue is lifted off from the bone as a sort of foreign body called an osteophyte, and in the growing, richly vascular periosteum, there appear osteoid trabeculae, which later become bone after taking up calcium. Then the richly cellular tissue between the trabeculae turns into marrow.

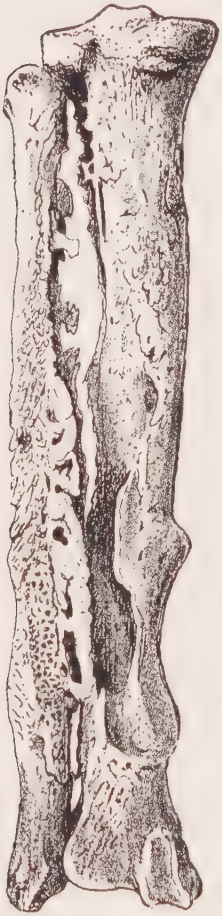


FIG. 539.—Immense osteophytes (ossifying periostitis) in leg ulcer; bridge-like synostosis of fibula and tibia; deep bone scar on the median surface of tibia; posterior aspect; about ¼ nat. size.

The osteophytes are porous in the beginning, pummice stone-like, richly vascular, and following partial calcification, are fragile, or tender; in these cases they are but loosely attached to the bone and may easily be rubbed off a macerated bone as though they were weathered mortar.

Osteoblasts later form bone from the marrow tissue; lamellated bone of good architecture is laid upon old, calcified, (meshed), bony trabeculae, until the pores of the osteophytes are gradually closed. Then the osteophytes become bony tissue of varying toughness, ivory hardness, firmly attached to the underlying bone like an icing; they thus become hyperostoses which often take the most bizarre forms, angular, stalactites, leaf-like, etc. Later, this sclerotic osteophyte may again be invaded by wide marrow cavities (medullization), and come to resemble spongy bone.

Diffusely spread osteophytes lead to general thickening (hyperostosis), or in flat medullization between old bones and the deposit of new bones, to the formation of scales, or a so-called double cortex (fig. 575); circumscribed osteophytes produce local thickenings of the bone (hyperostosis, exostosis).

Periostitis ossificans is exceedingly frequent. It develops after trauma, after irritation from the neighborhood, *e.g.*, a leg ulcer (fig. 539), or after various kinds of ulceration of the skin, caries and necrosis of the bones, arthridites, etc. For diffuse periostitis ossificans, see p. 1240.

A peculiar form may follow a cephalhematoma neonatorum (fig. 540). A cephalhematoma is a hemorrhage between the periosteum and the bones of the skull. It may be external or internal, *i.e.*, between the bones of the skull and the dura. It is much more frequent externally, is produced by tearing of periosteal vessels during crushing of the soft parts of the skull, or, less commonly, by fissures from protracted difficult labors. It may reach the size of an apple, is most frequent on the temporal bone, occasionally over both, more often on the right side if unilateral; here it takes on a spherical, hemispherical, or a kidney-shaped contour. More rarely the hematoma is situated on the forehead, or occipital bone where it is rounded. It never spreads over a suture. In the course of days, the edges of the uplifted periosteum (pericranium), form a bony wall or ring, *i.e.*, around the base of the hematoma, even while the "tumor" is still growing; this is a product of ossifying periostitis. Occasionally the entire inner surface of the loose piece of pericranium produces bone; this lies as a flat plate or a shell above the hemorrhage which may remain fluid for weeks. It then appears as though the bony vault of the skull itself was pulled apart by an exudate. After months the extravasation and the new bone formation disappear leaving a few irregularities. It does not correspond to particular situations of the skull as does the ordinary caput succedaneum; the latter also consists of a bloody edema of the scalp on the presenting part of the head and is, however, often combined with an actual cephalhematoma (Beck). According to the latest views, this structure is caused by pressure differences between the inside of the uterus and the external atmospheric pressure (Stumpf). But Nebesky believes it is due to the pressure of well defined narrow spaces such as the external os, muscular pelvic floor, etc. It has been known to become gangrenous

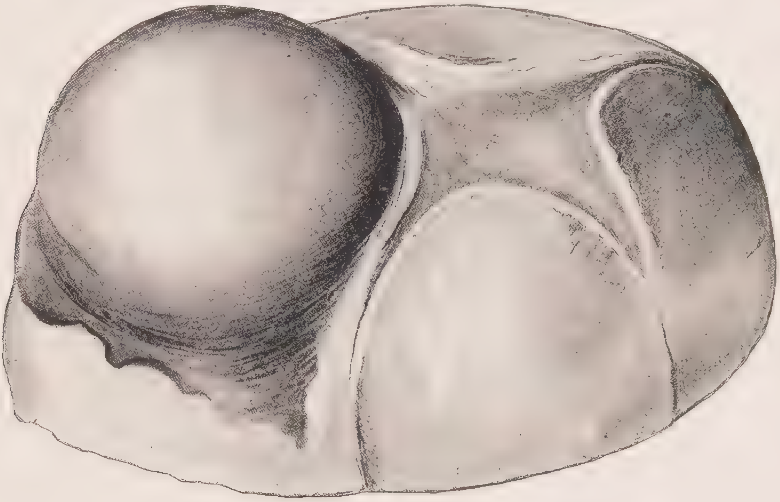


FIG. 540.—External cephalic hematoma of the r. parietal bone; to the right, large fontanell and frontal bone; newborn baby; 7/8 nat. size.

(Ehrendorfer). If infected, it undergoes suppuration, and leads to caries, necrosis and meningitis.

Various diseases accompanied by disappearance of bone often lead to a vigorous reactive ossifying periostitis, thus, tuberculosis, syphilis, and a number of tumors. Even the so-called pregnancy osteophytes should be mentioned; these occur as finely arborescent structures, particularly on the internal surface of the cranium, preferably along the longitudinal sulcus, in the region of the middle meningeal artery. Decalcification may lead to regression. According to Hanau, they are related to increased resorption in the bones (p. 1079); roentgenologically, Dreifuss found them in 33.3% of the living. A particular classification is merited by the periosteal new bone formation in osteomalacia (p. 1077) and in rickets. The relation of periostitis ossificans to the healing of fractures has been discussed on p. 1084. A periosteal callus is a particularly large, slowly ossifying osteophyte, with the further peculiarity, that it contains an occasional island of cartilage. Periostitis ossificans is an important process even in osteoplasty (p. 1082).

Furthermore, periostitis occasionally leads to synostoses; thus, most frequently, between two neighboring vertebral bodies, between the tibia and fibula (fig. 539), more rarely, in an entire foot, or ankle, or rib joint.

Periostitis Purulenta.—The most important form of this condition will be discussed under acute hematogenous periostitis and osteomyelitis. Pyogenic organisms may reach the periosteum directly through a wound, or may be carried through the blood stream from some other place in the body, thus adding infection to a trauma which has produced no external damage, but a locus minoris resistentiae.

The exudate collects in the delicate internal periosteal layer, and between this and the bone, thus lifting off the periosteum (periostitis purulenta dissecans), see fig. 541. It may invade the surrounding soft parts, and produce a phlegmon; these cases usually end fatally. The pus may, however, rupture externally, when the process is apt to heal with cicatrization. If the infection is of mild degree, granulation tissue is established in the periosteum, which may suppurate; with time, however, if the suppuration ceases or the pus is emptied externally, healing with cicatrization takes place.

The isolated processes in this condition will be dealt with more fully under acute osteomyelitis and periostitis.

Further results of a purulent periostitis are exfoliation of superficial layers of the bone, necrosis of larger parts of the bone robbed of their nutrition, and caries, all of which will be discussed in later chapters.

See p. 1102 concerning periostitis albuminosa.

Osteomyelitis and Ostitis.—From what has been said concerning ostitis and osteomyelitis, it is clear that inflammations established in the marrow cavity of tubular bones or in the vascular spaces of the spongiosa and compacta in other bones, show no fundamental difference. Osteomyelitis and ostitis may therefore be discussed as one. (Concerning the general diseases of the bone marrow in infectious diseases, see p. .290 Excellent presentation of osteomyelitis in "Erkrankungen der Knochen" by Anschutz.)

Acute Osteomyelitis and Ostitis.—The acute hematogenous infectious bone marrow inflammations, usually combined with periostitis.

The disease is based upon infection, wherein the organisms and their metabolic products, reach the vascular parts of the bone, *i.e.*, the marrow and the periosteum, by way of the blood stream. If the inflammation extends into the smallest spaces of the bone itself, the condition is known as ostitis.

Not rarely, there is coincident invasion of a joint, according to Lexer, particularly when the infectious organisms are streptococci and pneumococci.

The condition may be "so-called primary or spontaneous," beginning with pain and fever, preferring younger individuals, especially children, often when they are anemic, and when their bony growth is not as yet completed. When the surgeon speaks of acute osteomyelitis, he usually means this "spontaneous" form arising during childhood.

Not rarely these "spontaneous cases," may show some minor primary condition in another part of the body, such as a furuncle, a panaritium, a phlegmon, an angina, which is the portal of entry of the bone infection.

According to Trendel, the curve of frequency increases to the seventeenth year, and then falls rapidly; most of the individuals attacked were between the thirteenth and seventeenth years. The male sex is much more frequently the victim (trauma?). The osteomyelitis of sucklings merits a particular position inasmuch as streptococci are by far the most frequent invaders; the course is often very severe, and frequently accompanied by empyema of a joint (Haller).

In other cases, the disease is notoriously secondary to pyemic and infectious diseases, is therefore a metastatic inflammation or a pyemic metastasis in the ordinary sense; these infections are particularly: scarlet fever, measles, typhoid fever, recurrent fever, small pox, pneumonia, gonorrhea, etc.

Among the bacterial inflammatory irritants, the ordinary pyogenic cocci merit first consideration.

Particularly in primary spontaneous acute osteomyelitis and periostitis, pyogenic cocci should be suspected; in these conditions, as a rule, the staphylococcus pyogenes aureus, or the albus, can be found in the foci of the bones, and occasionally in the blood intravitam (Garre).

The streptococcus may also be mixed with these organisms; according to Lexer, the streptococcus pyogenes is often the only organism present.

K. Muller and Klemm believe the classical picture of osteomyelitis is produced only by staphylococci, inasmuch as infection with streptococci, pneumococci and typhoid bacilli, produce changes in the symptom-complex. Klemm holds that osteomyelitis streptomycotica is less severe, more apt to have cortical foci, or foci in the epiphyses or the epiphyseal borders, so that loosening of the epiphyses and exudation into the joints are frequent. The severe progressive marrow phlegmons of classical osteomyelitis are said, however, not to occur. The neighborhood of the parts is edematous and shows a tendency to undergo gangrenous destruction, whereas in staphylococcus infection the tendency is more toward suppuration.

Secondary metastatic osteomyelitis and periostitis are produced by the same organisms which cause the primary disease, viz., typhoid bacilli, pneumococci, alone or helped secondarily by staphylococci or streptococci (puerperal fever, umbilical sepsis, scarlet fever, diphtheria), etc.; colon bacilli occasionally play an etiological part; in other cases there is a septic mixed infection, *i.e.*, the simultaneous presence of specific and ordinary pyogenic organisms.

There are bone involvements in typhoid fever, in which only typhoid bacilli are found in the pus from the bones (p. 796). Pure typhoid pus is a yellow brown, rust colored fluid. This infection, as a rule, shows no tendency to spread, as long as no secondary infection is added (Lexer).

The specific typhoid, usually cortical, bone inflammations show various types according to the relationship of absorption, caseation (wherein dry granulations similar to those in tuberculosis occur), liquefaction or —rare—the formation of a central osteomyelitis with sequestrae. In fatal typhoid fever, Quincke and Stuhlen cultured the bacilli from the macroscopically unchanged bone marrow of the ribs and the sternum (compare the findings of Eug. Fraenkel in bone marrow, p. 290). Quincke also records cases of spondylitis typhosa, and emphasizes certain clinical peculiarities, particularly its relative benignancy, mild tendency to suppuration and necrosis, tendency to subacute course, and to long latent periods. Thus, for example, typhoid organisms remained viable in the cases of Sultan and Buschke, (periostitis typhosa) six and seven, in Tubby and Braxton Hicks's cases even 13 years after recovery from the disease; see also Fogh. Metastatic rib cartilage necrosis occurs in typhoid fever (but also in other infectious diseases). According to the author's experience, this seems to be more common than is taught (Herzbecker, lit). For necrosis of the lower jaw, see p. 1116.

The Etiology of Acute Osteomyelitis and Periostitis. Experimental.—The organized causes of inflammation enter the blood stream and are deposited in the marrow or the periosteum. The passage of bacteria into the blood from a primary portal of entry may occur without fever; in fact, the portal of entry, *e.g.*, a panaritium, or a furuncle, may even be healed by the time the bone metastasis has manifested itself clinically. Newer investigations (Eug. Fraenkel) have shown that corresponding bacteria may be found in the bone marrow in cadavers who at autopsy have panaritia, pneumonia, phlegmons, or erysipelas, without there having been a clinical blood infection with fever, chills, etc. From this it may be concluded, that bacteria reach the blood stream and the bone marrow quite frequently even from mild localized infections. In fact, it is known that bacteria enter the blood occasionally through intact external skin, intact mucous membranes (gums, tonsils, pharynx), and through the intestines, probably only when they are very virulent. For the production of a suppurative focus in the bone, the bacteria must have a high degree of virulence, and be present in large numbers; otherwise they are removed. Previously it was thought that trauma played a great part in helping localize the infectious organisms in the bone. Experimentally, osteomyelitis and periostitis can be produced by subcutaneous injury of a bone, (Becker, Krause, Rosenbach), or after ligation of an extremity in young animals (Ullmann), and simultaneous injection of microorganisms of various kinds in the blood, particularly the ordinary pyogenic cocci with their metabolic products. The present opinion is, however, that trauma is important in reducing the bactericidal ability of the tissues, so that bacteria already present or brought there shortly after the injury, are able to multiply vigorously. Then the opinion was expressed that the hyperemia of the growing bones of younger individuals was the necessary predisposing cause, and this osteomyelitis was called the pyemic localization of the growing period. Most of the animal experiments yielded results confirming this point of view. In young animals (*a*) it is possible to produce an acute osteomyelitis localized similarly to that in humans, merely by the injection of staphylococci, with no injury (Rodet, Lexer). The animals die from pyemia in from eight to ten days. (Severe degeneration of the kidneys.) The foci are most numerous in the neighborhood of those parts of the cartilage in which there is the more active growth (Jordan, K. Muller, Lexer and others), *e.g.*, the spongy ends between the epi- and diaphyses (have been called by Kocher, the metaphyses). This part has an independent supply of vessels entering from without, and branching toward the cartilage. The two other vascular regions of the long bones are supplied by the nutritional artery in the middle of the diaphysis, which branches upward and below to the metaphysis, the epiphyseal vessel coming from without, and spreading to the bone nuclei of the epiphysis (Lexer, lit.). The epiphyseal and metaphyseal vessels are end arteries (Langer). These vascular areas are sharply and markedly developed only in very youthful bones. Therefore, the lodgement of infectious organisms floating around as emboli is very easy in richly vascular young bones (see also experiments of J. Koch, lit., Kubo). Later, the arteria nutritia becomes much less important than the short epi- and metaphyseal arteries of the ends of the joints. In older animals (*b*), on the other hand, there is produced a multiple pyemia with localization in joints, muscles, internal organs, as in the pyemia of adults. In later researches with less virulent cultures of staphylococcus aureus, and albus, and streptococci, Lexer succeeded in producing a long lasting suppurative process similar to the spontaneous osteomyelitis of humans; he was confirmed in his results by Dumont (lit.), who amplified them by microscopically demonstrating the first localization in the very smallest metaphyseal vessels. Pneumococcus injections into the blood stream of younger animals (rabbits), were always followed by acute septicemia and death (Bolognesi, lit.).

In acute spontaneous osteomyelitis and periostitis, the disease attacks a single long bone—most frequently femur, tibia or humerus—or several at the same time, or following each other, inasmuch as the first focus may produce further metastatic lesions. More rarely, the short flat bones are involved (clavicles, scapulae, ileum, calcaneum, bodies of the vertebrae, ribs, bones of the skull). The process begins in the periosteum or in the bone marrow, and in the long bones preferably in the spongy, richly vascular metaphysis.

See Trendel concerning statistics of the localization in the various parts of the skeleton.

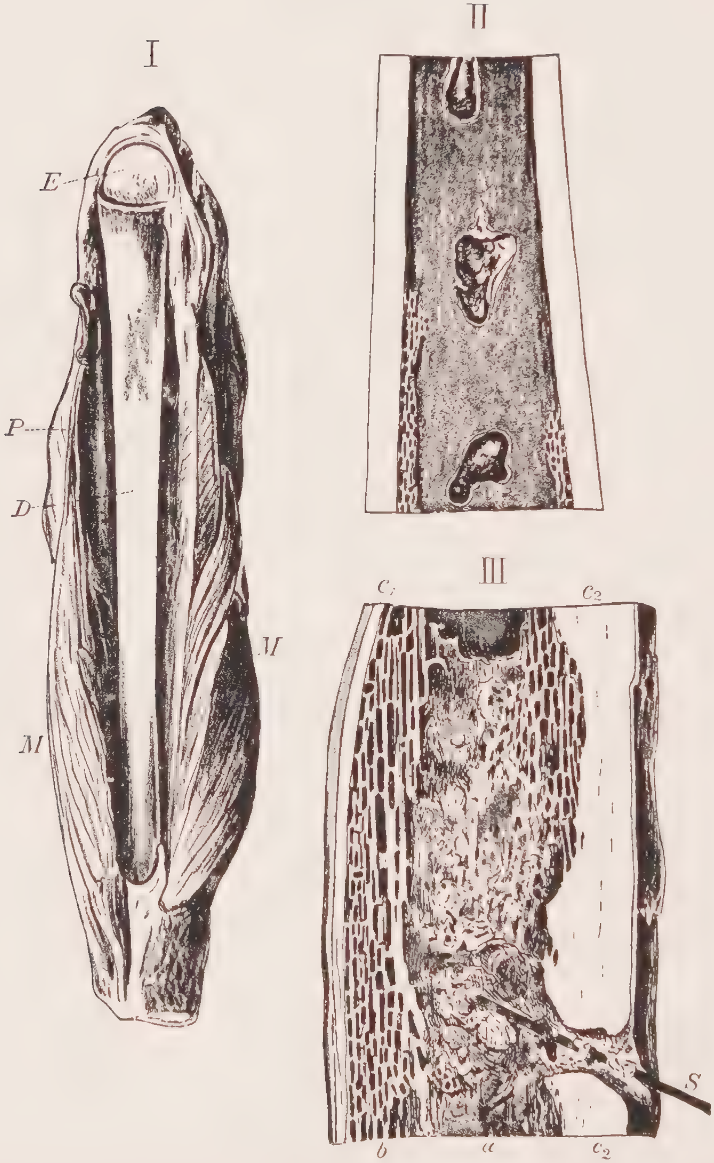
See Donati and Volkmann, (lit.) concerning the rare acute and subacute osteomyelitis and periostitis purulenta of the vertebrae, from which occasionally a secondary osteomyelitis in other bones may arise. Rare osteomyelitis of the patella is described by Partsch (portal of entry of the infection, a carbuncle of the lips). For discussion of the importance of the blood-forming marrow in the acute infectious diseases, and the peculiar differentiation in relation to the marrow of the vertebral bodies with 90%, and the long bones with 10% finding of bacteria, see under bone marrow (p. 290) and E. Fr. Muller.

Acute periostitis begins with an inflammatory hyperemia, serous or fibrinous exudation, and cellular (suppurative) infiltration. The reddened, juicy, thick periosteum can be lifted from the bone more easily than usual. The suppurative infiltration increases; masses of red blood corpuscles (hemorrhages) appear in the exudate. The tender, internal, so-called cambium layer of the periosteum is saturated with pus, which accumulates between the periosteum and the bone. Thus the former becomes ribbed in certain situations (subperiosteal abscess), or is lifted off and deflected from the bone (periostitis purulenta dissecans). On section the naked bones are covered with pus (p. 1100, illus. I).

An extensive separation of the periosteum takes place in periostitis maligna or acutissima, in which the exudate becomes ichorous. The periosteum may be very brittle or tender and discolored gray green. In a very short time the entire shaft is denuded and surrounded by a cloak of pus. After rupture of the periosteum the suppurative or ichorous inflammation spreads into the soft parts as a phlegmon, particularly into the interstices of the muscles and the subcutaneous tissue, and may even perforate externally. The muscles themselves may be peppered with innumerable abscesses. This malignant form usually causes death from septicemia or pyemia, very often with suppurative thrombophlebitis.

The periosteum, or the bone from which the periosteum has been removed, undergoes necrosis since its nutrition is entirely cut off. The removal of nutrition from the external periosteal surface alone is sufficient, as a rule, to produce merely superficial necroses; more extensive necrosis, which occasionally involves an entire shaft, even an entire bone, occurs only when actual endostitis is present, and the pus, following the vessels, extends into the intraosteal spaces, the Haversian canals, and perhaps to larger marrow cavities. There may also be a coincident thrombo-phlebitis of the vessels of the bone marrow. The necrotic bones are white and smooth. But if granulation and suppuration produce defects in the canals, the bone appears devoured, porous, and the condition is known as caries.

Acute osteomyelitis begins with hyperemia of the marrow, finally accompanied by hemorrhages, and quickly followed by the formation of inflammatory foci, most numerous around the diaphyses, and the zones around the epiphyseal ends; from here it spreads into the shaft, the epiphyses, and into the joints. At first the exudate is serous or fibrinous, but it soon becomes purulent or ichorous, the foci take on a cloudy yellow or green color, while their surroundings become intensively red. When the organism is less virulent, circumscribed abscesses are formed, which may become encapsulated (p. 1100, II). Otherwise, the suppurative inflammation takes the form of a phlegmon, more infiltrating than liquefying, and spreads quite diffusely (osteomyelitis maligna). Complete obstruction of the vessels produces necrosis of bony parts (central necrosis), or (perhaps from toxin effect) sequestrae of the marrow, which may lie in the phlegmonous marrow, or in pus cavities (p. 1100, II). In severer infections the



FIGS. 541–543.—I. Acute suppurative periostitis and osteomyelitis, with total necrosis of the r. fibula. The osteomyelitic foci (shining through as dark markings) are located in the upper portion or the diaphysis. Detachment of upper epiphysis (E). There were also osteomyelitis and periostitis of the tibia; phlegmons of surrounding soft tissue; metastatic foci in a rib and l. radius. Child 1½ years old died of pyemia. D, diaphysis; P, detached periosteum; M, muscles; ½ nat. size. II. Encapsulated abscesses in bone marrow with formation of small sequestrae of marrow. Central part of the diaphysis of femur of a man 21 years old; ½ nat. size. III. Osteomyelitis existing many years in the lower portion of shaft of r. femur sawn longitudinally with cloaca formation backward; S, probe in cloaca. Considerable hyperostosis, partly spongy (b) partly sclerotic. At C2, sclerotic cortical thickening; Cl, thinning of cortex, much spongy bone has formed from there inward. The marrow cavity a, is invaded in the upper portion by spongy bone tissue; otherwise it is filled by fibrous and granulation tissue containing small spongy sequestrae. Man 45 years old died of pneumonia; ½ nat. size.

suppuration spreads quickly from the marrow through the Haversian canals of the corticalis, to the periosteum. This is then infiltrated with pus and separated from the bone, the subsequent course of events being as in primary periostitis. If the marrow and the periosteum are both diffusely and seriously involved (panostitis), total necrosis of an entire bone may occur without actual endostitis. When the epiphyses of young bones are particularly full of foci, or when the diaphyseal foci reach the epiphyseal border, the diaphyseal cartilage (intermedia cartilage) is destroyed, and the epiphysis itself is lifted off, even in a few days (figs. 541–543 I).

This loosening of the epiphysis is possible until about the twentieth year; after this, the cartilage between the diaphysis and the epiphysis disappears since it is no longer necessary for the growth in length of the bones. Shortening and abnormal mobility are the results of this loosening.

Very frequently a sero-fibrinous (so-called sympathetic) exudation takes place into the neighboring joints, but if pus accumulates, severe and permanent changes may be produced in these structures.

Consequences of Acute Osteomyelitis and Periostitis.—In the majority of cases, the generalized severe febrile symptoms regress, and the process localizes to the diseased bone. If the suppuration followed by necrosis is very chronic, the individual may die many years later from amyloid degeneration of the internal organs, perhaps with ascites and anasarca. But if a number of bones are involved from the very beginning, the pyemic infection is quickly fatal. Metastases from osteomyelitic foci may be manifested in other bones, as well as in the internal organs, particularly the lungs, kidneys, heart, and also the skin (metastatic abscesses). Death usually follows in a few days or weeks from the generalized infection. Transfer is by means of septic thrombi in the veins of the bones (osteophlebitis), which may spread, *e.g.*, from the femur to the deep femoral veins or the iliac vein. Necrosis, and the formation of sequestrae are very frequent consequences of osteomyelitis and periostitis. They will be described more fully in a particular chapter (p. 1116). Healing without bone destruction after resorption of the inflammatory exudate is still possible in the beginning stages of the disease.

A seeming healing, or periodic exacerbations, perhaps even a continuous process with severe neuralgic pains, are characteristic of the chronic forms of sclerosing osteomyelitis, in which operation reveals a so-called central abscess in the diffusely sclerosed metaphysis. The bone may be elongated and diffusely thickened. The differential diagnosis from sarcoma, especially when the course is insidious, may be very difficult as the author can testify from examining amputated thighs in a number of cases (Klemm, and see also p. 1102). But the marked osteosclerosis and the abscess serve, as a rule, to differentiate roentgenologically, the process from tumors and cysts (Anschutz).

Traumatic Osteomyelitis and Periostitis.— These follow infections from operations, gun-shot wounds, complicated fractures, or amputations.

The Rarer Forms of Acute Osteomyelitis and Periostitis.—(*a*) Periostitis albuminosa or serosa (Poncet, Ollier), is usually an abortive form of suppurative periostitis, and is merely a different degree of the same process (Schlange, Vollert). In some of the cases, tuberculosis is said to be at its basis (Garre, Sleeswijk). The exudate contains a large amount of albumen; according to v. Volkmann, it is a mucoid degeneration of pus cells, but, according to others, (Kocher and Tavel), it is caused by a granulation tissue undergoing fatty degeneration, surrounding the serous exudate. J. L. Burckhardt saw many fatty plasma cells, and also many Russel's bodies (p. 301). Staphylococci have been found in the exudate of cases of the first type, (as in spontaneous acute periostitis and osteomyelitis), probably, however, of decreased virulence; according to Heinemann, the exudate may measure two liters. The same causes are probably at work in those which run subacute and chronic courses. According to Schlange, cysts containing serous contents may appear in the marrow (analogous to bone abscesses); see also under ostitis deformans, p. 1107. Concerning traumatic genesis, see Heinemann, lit.

(*b*) Sclerosing non-suppurative osteomyelitis (Garre), is rarer; Kocher and Tavel believe it is a proliferating (non-exudative) osteomyelitis, in which they differentiate a vascular, a granular, and a sclerotic form.

(*c*) Sarcoma-like dry forms (Kocher and Tavel, Jordan), externally similar to syphilitic hyperostoses, may present differential diagnostic difficulties, even at microscopic examination, (p. 1101); to add to the pitfalls, it is known that a round cell sarcoma may arise in an old osteomyelitis (Klemm). To avoid mistakes, especially in small bits of tissue removed for diagnosis, it is best to consider that sarcoma can be diagnosed only when a well known form, *i.e.*, round, spindle, or giant cell sarcoma,—completely dominates the picture and there are no transitions from richly vascular granulation tissue to connective tissue. (Careful low power examination should be made first; many situations should be examined! Helps in the diagnosis are the demonstration of pyogenic cocci, the emigration of leucocytes in granulation tissue, and clinically, the finding of a typical sequestrum, Jordan.)

(*d*) Occasionally, many years after the acute stage of an osteomyelitis has disappeared, there are local recurrences in the same bone from persistence of the organisms (see Ehrich and the case of Fogh, of post-typhoid suppurative osteomyelitis of the femur lasting for twenty-three years with non-active intervals of months or years), or it is a reinfection (Kraske).

In addition to the abscesses, in infectious diseases there occasionally occur anemic necroses in the marrow, which are produced by embolic vessel obstruction.

Chronic Osteomyelitis and Ostitis.—The fundamental processes in these chronic inflammations can be resolved to destruction and construction of bone. Not rarely, both processes occur simultaneously. The various forms are:

Rarefying Ostitis (Inflammatory Osteoporosis).—Instead of the normal marrow tissue, that present is a richly vascular granulation tissue (ostitis granulosa), which spreads into the marrow cavities and the Haversian canals at the cost of the bony substance. The melting of the bone occurs without suppuration, in one case, from lacunar resorption, whereby the Haversian canals are dilated to Haversian spaces, and the compact bone becomes porous; in other cases by canalization, *i.e.*, by the formation of perforating canals. The sites of election are the epiphyses of the tubular bones, and the spongy parts in general.

The etiology of this ostitis is not uniform. Some cases are independent diseases and belong to an osteomyelitis of a dry, granular form (see above); others occur in conjunction with tuberculosis, lues, leprosy, (see under these diseases), in which the granulation tissue, however, has its own specific character; in still other cases, it is a minor secondary process in the loosening of sequestrae, and in necrosis. It may occur in the spongy parts of a callus, and of osteophytes. Its relation to the healing of bone wounds is of greater importance (the granulations growing from the bony canals undergo ossification at a later time). The same process is also met in caries, particularly as a fungoid caries, known as chronic granular ostitis with bone disappearance.

Caries of Bones. Chronic Intraosteal Granulation. Overgrowth with Solution of Bone (Billroth).—By caries is understood an interstitial intraosteal overgrowth of granulation tissue producing ulceration of the bony tissue, of a progressive chronic character, leading to more or less complete solution of the bony tissue with defects. The actual bone remains quite passive during this process of solution. Caries may be acute, *e.g.*, in conjunction with an acute osteomyelitis or other general infectious diseases, or it may be insidious, with suppuration or softening, -the usual form—or without these secondary accompaniments. Suppuration may also be a secondary symptom of caries, but it is not a necessary concomitant (Billroth). But for the development of a defect it is necessary to have active participation of granulation tissue. It may be simple non-specific, or specific, such as tuberculous, syphilitic, actinomycotic (simple and specific caries). Particularly in syphilis and occasionally also in tuberculosis, the caries may not produce one drop of pus (caries sicca).

By far the most frequent and important form of caries is the tuberculous type, which is called by many, but incorrectly, true caries.

For those forms in which the granulation tissue is particularly exuberant, (caries granulosa, carnosa and fungosa, the latter in the sense of an ostitis tuberculosa), the characteristics hold good which we have discussed under rarefying ostitis (p. 1103). But the granulation overgrowth, as a rule, spreads beyond the rarefaction, and produces actual defects; the bony tissue is entirely pulled apart.

In the specific forms accompanied by vigorous production of pus, the defects are not always so complete. Where the granulation tissue is less viable, the tearing apart of the bony tissue is also not so complete. Vigorous suppurative infiltration, softening, or other regressive changes such as caseation may so lower the absorptive ability of the granulation tissue that but little bony substance is brought into solution. The dying intraosteal new growth produces necrosis or death of the bony tissue by interfering with its blood supply. As Billroth says, there is a kind of maceration of the bone within the living organism; dead particles, usually of small size, are found between the inflammatory and the destructive products. Volkmann calls this necrosis or destruction of very small parts of a bone, molecular necrosis. They are partly decalcified, and when present in tiny particles, constitute bone sand. The latter is not constant in caries, but only occasional, and, as stated above, occurs in such forms which are accompanied by suppuration, or by an overgrowth of cells which compromise the vessels, or by caseation; it is constant in tuberculous processes in which such large sequestrae are formed that the condition has been called caries necrotica.

If the condition is examined more closely, we see, for example,—to discuss a very frequent form—the spongiosa laid bare from a suppurative arthritis which destroys the joint cartilage, whereupon the hyperemic, granulating marrow tissue produces pus (osteomyelitis or ostitis purulenta). This is called an open bone ulcer, or simple caries in contrast to fungoid caries. The pus may so fill the internal spaces of the bone that the blood vessels are compressed, the nutrition is cut off and the tissue becomes necrotic. The bone cells undergo fatty changes. At times, dead trabeculae of the bare spongiosa may remain connected with each other and in communication with the living bone, even after the superficial layers of the endosteal soft parts undergo complete liquefaction. The soft parts decompose within the bones, and the dead trabeculae are at least partly decalcified.

If we ask about the further fate of bony tissue in suppurative or ichorous ostitis, the answers differ, according to the author. According to v. Volkmann, the bony tissue is partly dissolved chemically, appears "weathered" like a stone, as it is subjected to molecular necrosis, and finally disappears into a powdery dust. v. Volkmann, and others, call this molecular necrosis a suppurative caries, while Billroth, whose idea we have adopted in general, insists upon the functional activity of the granulation tissue. Billroth insists that the name caries should be applied only to bony defects produced by lacunar solution, but this process may become complicated by necrotic processes, when, as mentioned above, there is vigorous pus production, or when destruction or a specific regressive change (caseation) occurs which reduces or removes the ability of the granulation tissue to resorb bone.

Caseous bones if also suppurative, appear dirty green. The spongy parts are soft, compressible and can be cut with a knife. When macerated, they are roughly porous, show defects as though they had been devoured, or as though worm-eaten.

A very important localization of simple caries must still be mentioned, namely, in the temporal bone. Chronic middle ear inflammations are usually the points of origin. Naturally, these are sometimes tuberculous, but more frequently are simple inflammations coming from the nasopharynx, or via the hematogenous route in infectious diseases particularly in childhood. The acute exanthemata must be especially emphasized (p. 607). Chronic middle ear inflammations run their course with the formation of granulations and more or less suppuration, in other cases with the formation of the so-called cholesteatomas in the cavities, and may produce extensive caries and necrosis of the bony parts. When these cholesteatomas are formed, the chronically inflamed mucosa takes on the character of epidermis. This is often called metaplasia of the epithelium (change of cylindrical epithelium into squamous epithelium, v. Troeltsch), but in most instances it is merely a covering of the granulating mucosa with squamous epithelium which spreads through a perforation in the drum from the external auditory canal (Habermann, Bezold, Haug and others). Cornifying squamous epithelial cells are compressed to leafy, concentrically layered, mother-of-pearl-like glistening, tumor-like bodies from the size of cherries to walnuts, which are mixed with cholesterin. Occasionally the centers of the clumps undergo softening, break up into small particles, and can be recognized by their detritus, the needles of margaric acid, and bacteria. A growing cholesteatoma may produce in the bone a smooth-walled spherical ulcer with a sclerotic border. In other cases, however, the bone becomes carious immediately with the formation of pus, which frequently becomes ichorous. This caries may be very extensive and lead to grave consequences. (Consult under inflammatory sinus thrombosis, pyemia, meningitis, brain abscess.) But true cholesteatomas also occur in the temporal bones; they are primary tumors from misplaced congenital epidermoid or dermoid germinal cells, as demonstrated particularly by Erdheim (lit.; see also Borchardt, A. Linck, lit.).

Ostitis (Actually Endostitis) Ossificans, Condensing Ostitis, Osteosclerosis.—This is the direct antithesis of osteoporosis, and consists of the formation of new, at first osteoid, then calcified true bone masses, coming from the marrow and vessel cavities and encroaching upon the old trabeculae. The spaces within the bone are filled with more and more bone tissue (fig. 544). This type of ostitis ossificans may lead to stony-hard thickenings, sclerosis, and eburnation.

v. Volkmann differentiates restitutive, reactive or indurative, and idiopathic bone sclerosis. Restitutive sclerosis sometimes follows a rarefying ostitis, whereby the thickened, previously light weight bone, becomes stony hard and heavy. An osteoplastic osteomyelitis also appears in the neighborhood of tumors which partly destroy the bone, etc., (see under bone tumors). The closure of marrow cavities after fractures, in amputation stumps, in the space left by discharged sequestrae, after osteotomy, etc., is due to this osteomyelitis ossificans (fig. 557). A reactive ostitis ossificans is very frequent, and is called forth by chronic inflammatory irritation; it is often combined with periostitis ossificans, so that there is a coincident thickening and an increase in the compactness of a bone. It may follow, among other things, chronic central osteomyelitis with the formation of sequestrae; it always occurs in the neighborhood of a bone abscess, or may follow a leg ulcer, or a chronic suppurative arthritis. Idiopathic sclerotic hyperostoses are rarer except in syphilis when they are relatively frequent. Phosphorus may produce an osteosclerosis (p. 1119), or an ossifying periostitis. The same is true of leukemia

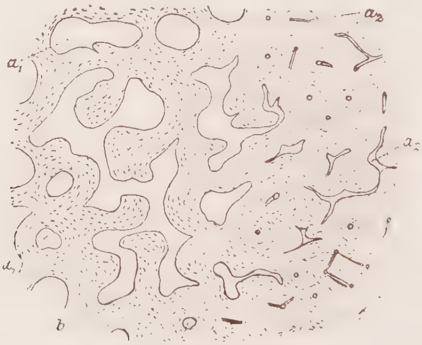


FIG. 544.—Osteosclerosis; a-1, wide marrow spaces, marrow tissue not indicated; a-2, bone deposit from marrow makes the marrow spaces of the diploe quite constricted; b, lamellated bone substance; from the frontal bone (thickened to 1 cm.) of a syphilitic woman. There was a slight dry caries on several places of the surface of the skull.

(v. Baumgarten, Schwarz and others); see pp. 204 and 1116. The name cyanotic hyperostosis may be used for those thickenings, particularly of the vault of the skull (details by Thoma), accompanied by cyanosis (heart failure, emphysema, etc.).

The Rare Forms of Idiopathic Hyperostosis.—Ostitis deformans (Paget's disease), and its relationship to ostitis fibrosa (v. Recklinghausen). In outstanding cases, Paget's disease is a very obvious clinical entity. It usually occurs in older individuals, and leads to gradually increasing softness, brittleness, and deforming thickenings of many parts of the skeleton, at first, and usually most marked in the tibia and the skull, (in which the bones of the face are usually not involved), the vertebral column and others. This leads to a decrease in the size of the body with changes in posture and gait (resembling that of a monkey). V. Recklinghausen recognized the anatomical foundation in a malacic process which he called ostitis fibrosa, consisting of changes in the architecture such as increased destruction of old bone, and vigorous production of new, but non-calcified bone in a fibrous ground work, which leads to enormous, extraordinarily variable changes in the skeleton. The same processes can be demonstrated in cases of generalized ostitis fibrosa which usually occur in adults, and the anatomic relationship with Paget's disease cannot be doubted in spite of isolated peculiarities (cysts and brown giant cell sarcoma-like tumors of the bones, marked and earlier changes in the femora than in the tibiae, less marked thickening of the skull, etc.). They are simply types of the same disturbance (Lotsch, lit.). There are all sorts of transitions from typical Paget's disease to other forms of generalized ostitis fibrosa. Ostitis fibrosa circumscripta is a particular clinical entity. It occurs most frequently, though not exclusively, in children and youthful individuals, (it is often seen in soldiers). There is a tumor-like fibrous ostitic local focus in a bone, usually a long tubular bone, but the joint is never involved; by softening it may produce a bone cyst. Another form of circumscribed ostitis fibrosa is represented by the so-called giant cell sarcoma epulis.

Paget's disease in its pronounced type, occurs in older and very old individuals. Thus in Stilling's cases the ages were 70, 77, 92 (for other figures, see Schirmer). Other cases of generalized ostitis fibrosa usually occur in younger adults; but there are transitions and exceptions. The disease usually begins insidiously; it may be accompanied by rheumatic pains. It usually involves a number of bones; in typical Paget's disease, the tibia is attacked first, and may show elongation; in other cases the femurs are first attacked, then the bones of the skull which remain free in only exceptional cases, then the vertebral column, usually with cervico-dorsal kyphosis, then the ribs, the sacrum, the pelvis, the latter of which sometimes shows deformities like those of osteomalacia, the lower jaw, which becomes broad and crooked; finally, practically all the bones of the body participate in the disease. In spite of this (exception ankle and wrist joints), there are usually no important changes in the hands and feet which serve to differentiate the condition from acromegaly. The so-called monosteal form of Paget's disease or ostitis fibrosa is relatively rare; in a case of Kuster, it occurred in one femur, in a case of Kockel, in both femurs. Cases in which the skull alone is involved are quite rare (Wrede and lit. by Frangenheim). The most frequent bone involved is the tibia, often but one. The skull increases in diameter, becomes four cornered, buckled, deformed, and too large for the small face; the hat becomes too small. The vault is more thickened than the basal part, although the base is hollowed out from the pressure of the brain against the anterior and middle fossae, while the surroundings of the foramen magnum following the counterpressure offered by the more rigid vertebral column, are pressed into the skull cavity, (kyphosis, elevation, convexobasia, P. Marie and Leri; platybasia, Regnault). The roof of the skull may reach the thickness of 2.8 centimeters, and in exceptional chronic cases observed by the author in the almshouse in Breslau, it reached the thickness of 4 centimeters, without leading to cranio-stenosis; the boundaries between the external table, the diploe and the internal table disappear completely. As recognized by the author in a case of generalized ostitis deformans occurring in a 36 year old gardener (fig. 546), the roof of the skull when fresh is of a

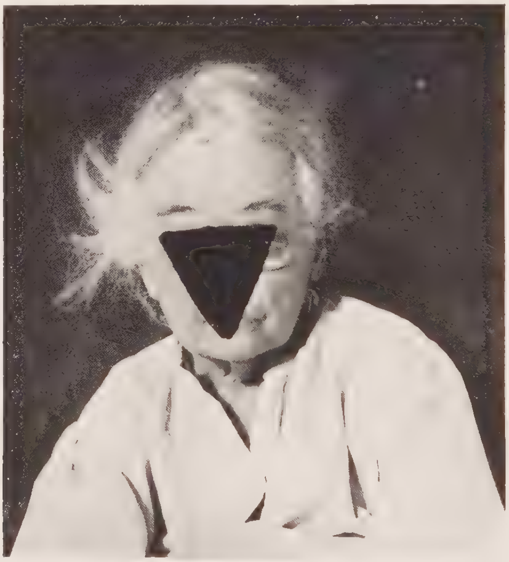


FIG. 545.—Paget's disease of the skull in a woman 70 years old. Present for many years. The patient was treated for a broncho pneumonia. X-ray plates showed typical thickening of the bones of the skull. L. H.

gray red spotted color, flexible like rubber, the dura is adherent, macerated preparations appear white, fragile, like pumice-stone, or "foamy," and as the skull in the collection in Basle shows, on touching, a finely powdered bone sand is removed. Nodular deformities and bending may occur, particularly in bones subjected to pressure; they appear slowly but steadily with increasing thickness, and are often accompanied by rheumatic pains, though this is not without exception. Since it involves particularly the legs and the vertebral column, the individuals become smaller, and take on a characteristic man-ape stature.

The condition is characterized anatomically (*a*) by extensive resorptive processes (Stilling, v. Recklinghausen and others) by which the bone disappears by lacunar resorption (and perforating canals?), but in pure cases not by halisteresis (according to O. Meyer this may sometimes occur). As v. Recklinghausen emphasized, in marked contrast to the conditions in osteomalacia, large numbers of osteoclasts take part. The bones become porous, brittle, particularly noticeable in the compact cortex. (*b*) In the diseased situations the marrow becomes fibrous, *i.e.*, the cells disappear, and the framework becomes thickened and fibrous. This is the primary occurrence. (*c*) A variable amount of new bone formation then occurs from the fibrous marrow (osteomyelitis fibrosa osteoplastica); connective tissue metaplastic new bone usually remains free of calcium or poor in calcium for long times; it is therefore soft, bendable and finely porous because its trabeculae are short and plump, and its spongiosa is narrow meshed. These processes take place simultaneously in the chronic disease, and the fact that the periosteum takes no part, is highly typical. To sum up, ostitis fibrosa is characterized by increased destruction, connective tissue metaplasia, which has been called by v. Recklinghausen, metaplastic malacia, reserving the name hyperostotic-metaplastic malacia for Paget's form. This new metaplastic bone has a lamellated structure and a large content of Sharpey's fibers, as does young connective tissue bone (p. 1057). In its further course the new bone may also be destroyed, but this is not a necessary procedure. There are also porous hyperostotic and sclerotic forms (Christeller), according to whether the destruction or the construction and the content of calcium predominates. If a young individual is attacked by the disease, endochondral ossification may be completely destroyed from incomplete calcification and from the inability of the fibrous marrow to produce cavities; thus there is a macroscopic similarity to rickets (pseudo-rickets, see Christeller). In older individuals predominance of the destructive process calls forth pseudo osteomalacic forms. Rarely, a true osteomalacia appears late in the disease, as in the case illustrated, fig. 524; according to O. Meyer, the histological changes are fundamentally the same, but see, for the contrary, Christeller.

The marked destruction and the increased construction produce a total rearrangement of the internal architecture, a deforming transformation with softness, bending, thickenings, and even elongation of the plump bones, which thus take on a monstrous appearance (see the femur shaped like a shepherd's crook illustrated by v. Recklinghausen). In x-ray pictures the boundaries between the bones and the soft parts become obscure. Fractures are not rare (Glaessner, v. Recklinghausen, O. Meyer). In the

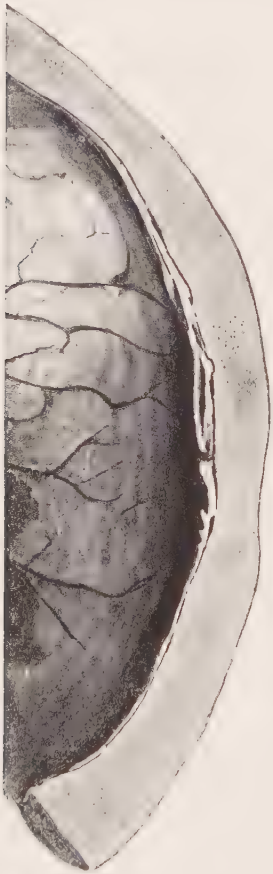


Fig. 546.

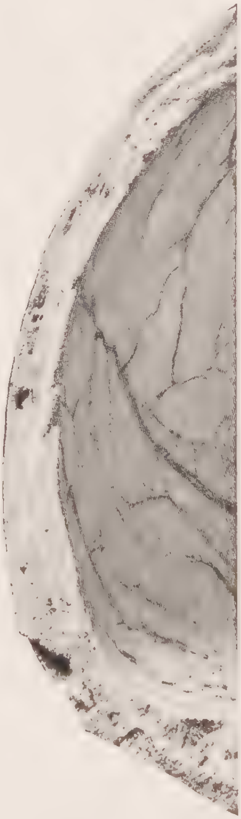


Fig. 547.

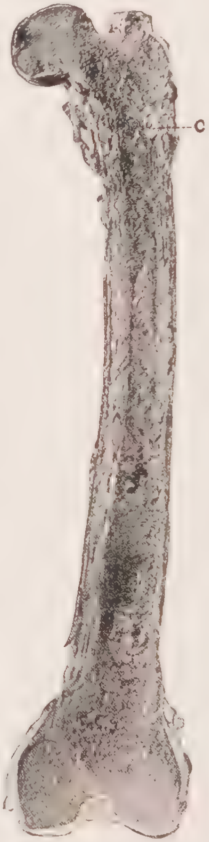


Fig. 548.

Fig. 546.—Fibrous ostitis (deformans); portion of posterior lateral roof of skull. Bone markedly thickened (up to 1.5 cm.) gray red, flexible; man 36 years old. Comp. femur, fig. 548; preserved in formalin.

Fig. 547.—Fibrous ostitis (deformans); portion of posterior lateral roof of skull. Pumice stone condition of bone which is markedly thickened and falls into dust on touch. Specimen dried after maceration.

Fig. 548.—Fibrous ostitis (deformans); crooked, irregularly thickened l. femur; complete modification. Bone cortex thick, peculiarly long striated, roughly porous, marrow impregnated, dark gray red in color. The marrow cavity is also partly filled with roughly porous bone tissue. C, small cyst with smooth inner surface and fibrous wall; man 36 years old. (See Fujii, D. Z. Ch. 114, 1912.)

case described below, the author saw two transverse fractures of the left humerus, fracture of the pubic bone, and the neck of the left femur (36 year old man).

The fibrous marrow occasionally resembles a fibroma (see the case of Schlange-Axhausen), which replaces the bone.

Among secondary changes in the marrow may be mentioned: (*a*) regressive changes consisting of focal liquefaction and the formation of cysts; smooth-walled, occasionally multilocular spaces containing a serous or pasty content, appear as "cystofibromas." Thus in a right humerus, 34 centimeters long, from a 36 year old man, who had small cysts in his left femur, illustrated in fig. 548, the author saw a smooth-walled cyst as thick as a thumb and 12.5 centimeters long, containing watery contents. Most of the solitary bone cysts in the long bones as described by Schlange, and which are observed quite frequently, usually in the femur, humerus, the tibia and the fibula (fig. 644), are probably the result of a circumscribed ostitis fibrosa (Fujii); they may lead to spontaneous fractures. On the other hand, there also occur: (*b*) progressive changes in the form of small, circumscribed, blood pigmented, rusty brown or brown red giant cell sarcoma-like tumors, some of which have been described as actual metastasizing giant cell sarcomas (v. Haberer); these grow here and there in the fibrous osseous framework (Schonenberger, lit., Platou), particularly in the cortical parts of the diaphyses, which are subject to particular mechanical irritations; by hemorrhage they may become cysts. These "brown tumors" as productive reactive new formations must be differentiated from true sarcomatous blastomas (Konjetzny, Molineus and others). The typical epulis (p. 573) is also considered by v. Recklinghausen in this classification; this reactive giant cell overgrowth is almost always unilateral, and reaches its development in a fibrous ostitic focus; v. Recklinghausen calls this "the highest degree" of the fibroostitic new formation. (Boit, on the other hand, believes that these epuli are true blastomas.) In other parts of the same bone the marrow may be fatty or gelatinous.

The etiology of the disease is obscure. Arcangeli is of the opinion that it is an infectious process, and utilizes the results of Bignami, who demonstrated the same organisms in ostitis deformans (Paget) as found by Morpurgo in rickets and osteomalacia, namely, a Gram-positive diplococcus. Lannelongue and others think of syphilis (Schirmer, lit.). Relations to the internal secretory glands have also been postulated (see particularly the parathyroids, O. Meyer), as well as neuropathic influences. But as opposed to these ideas, it frequently happens that only isolated parts of the skeleton are involved, and those parts are fortuitous and without rule. Stumpf in assuming a relationship to rickets, calls it a metarachitic disease. Lit. in appendix.

See Ingier, Pick, concerning the resemblance of the snuffles of mammals to ostitis fibrosa.

Hyperostosis cranii, craniosclerosis or leontiasis ossea (Virchow), is a rare disease found usually in younger individuals, producing enormous, diffuse hyperostoses beginning usually in the bones of the face and then extending to those of the skull. Erysipelas, traumata, tear sac suppurations figure as etiological factors. Finely porous thickenings, and after completed calcification and sclerosis, ivory-like or "marble hard" exostoses of wavy lobulated appearance are present, particularly in the bones of the face, especially the lower jaw (see H. Burckhardt), the lower edges of the orbits, in the region of the molars, all of which justify the designation leontiasis (Virchow, who had in mind a comparison with leprous leontiasis). The cavity of the skull, the cavities of the face, as well as the fissures and foramena become very narrow (cranio-stenosis). Headaches, cramps, paralyses, neuralgias, blindness, disappearance of the sense of smell, deafness may follow. The weight of the dry skull, normally about one

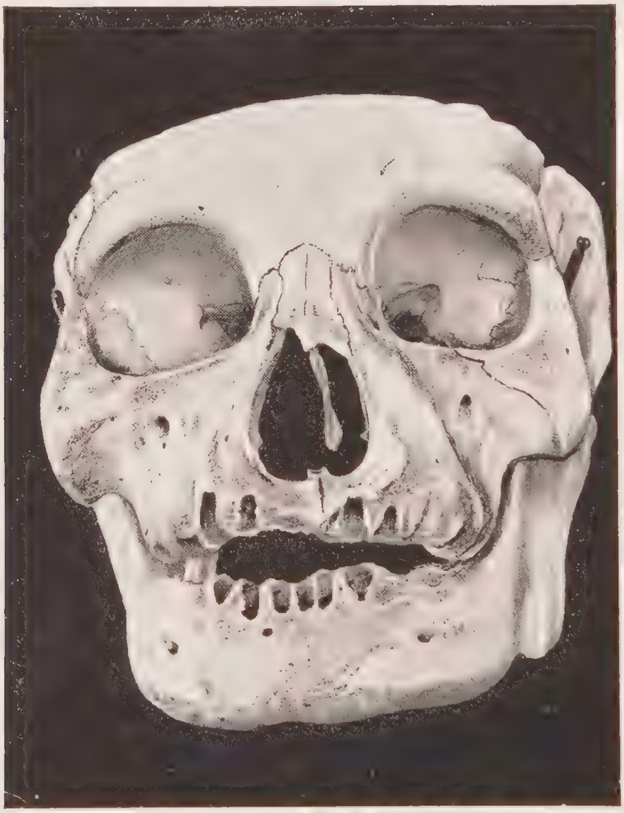


FIG. 549.—Osseous Leontiasis; pumice-stone character; 8/13 nat. size.

kilogram, may be more than five kilos; the roof may become three to four centimeters thick. P. Marie, among other things, calls attention to the fact that the hands and feet become hypertrophic, and that the vault of the skull may be unchanged, both in contrast to ostitis deformans. Paget also insists upon a sharp differentiation of the two. M. B. Schmidt (lit.), Bockenheimer, Boit, Lotsch, Koch on the other hand, more or less firmly believe in the identity of leontiasis ossea and ostitis deformans (of Paget). v. Recklinghausen also would classify the condition under hyperostotic metaplastic malacia or ostitis fibrosa hyperostotica. We must then assume that the stony-hard, thick skull is a healed, stationary case, which was once florid and cuttable, and that this soft stage may last for decades without leading to craniostenosis (see the observation of the author, p. 1108). Even though many cases of leontiasis ossea belong to the type ostitis deformans, nevertheless the interesting observation of Nauwerck shows that syphilis may produce the macroscopic picture of leontiasis ossea without, however, histological analogies to ostitis deformans. Frangenheim (lit.), on the other hand, reserves the name leontiasis ossea for diffuse hyperostoses of the skull and bones of the face, and believes in a differentiation of ostitis fibrosa, ostitis deformans and familial hyperostosis of the jaw (see below). A sclerosing hyperostosis of moderate degree is quite frequent in chronic alcoholism, in heart and kidney diseases, accompanied by chronic venous hyperemia of the skull and the meninges; the dura is often tightly adherent to the skull in these cases.

Concerning familial hyperostosis of the jaw from bone hyperplasia caused by an inflammatory hereditary foundation but the etiology of which is unknown, see Frangenheim. [A classical specimen of leontiasis osseae is deposited in the museum of the University of Liverpool. See Knaggs, R. L., Brit. J. Surg., 11: 347: 1923.—*Translator*.]

Acromegaly (Marie) or pachyacria (v. Recklinghausen) is as yet incompletely explained in its pathogenesis; it usually occurs in younger individuals, but never in childhood; as a rule, not before the third decade; it develops as an irregular thickening of certain pointed parts of the body, particularly the bones, but also the soft parts. The hands and the feet, lower jaw, lip, tongue and nose are all increased in volume. Subperiosteal and subcortical bone formation produce even increases in the thickness of the bones (not in length) (Arnold); at the same time they become covered with exostoses; internally there is usually a predominance of resorptive processes; sclerosis can seldom be demonstrated, (Dietrich, Beneke). The hands take on a paw-like appearance, they are four cornered, as though upholstered, shovel-shaped; the fingers are sausage-shaped, their ends are four cornered, the nails are broad, short and ribbed; the feet take on an elephantic appearance. The lower jaw enlarges, the chin protrudes in a characteristic way (progenia), the lower part of the face becomes broad, the angles of the jaw are stretched, and the teeth become separated (Strumpell); figs. 550 and 551. (Concerning this diastasis of the incisor teeth and others, see Kloeppel.) The hypertrophic tongue protrudes between the teeth. The alveolar rim is thus bowed as in other macroglossias (Arnold). In isolated cases the vertebral column becomes kyphotic. The external occipital protuberance may also be markedly developed. Involvement of the organs of sight is relatively frequent, either as a complete amaurosis, or merely diminution in the vision (Uhthoff, Greeff).

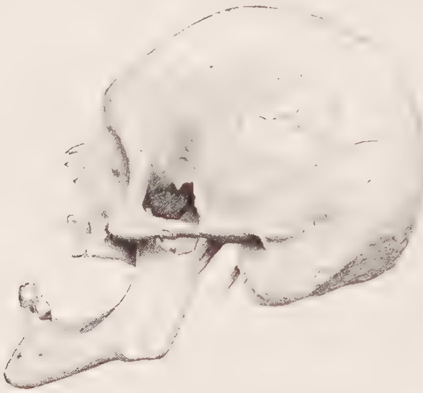


FIG. 550.—Skull of an acromegalic giant over 2 m. tall, 49 years of age. Excessive growth of body began in his 20th year. Measurements: sole of shoe, length 34 cm., width 12 cm.; skull weighed 1070 gms.; circumference 55 cm.; weight of lower jaw, 145 gms. Statements in reference to the dilated sella turcica and the extreme dilatation of the pneumatic cavities of the skull in chapter "hypophysis."

The etiology of acromegaly is related to the hypophysis, viz., to hyperpituitarism (lit. by P. Marie and Leri), the cardinal symptoms of which are represented by the triad: diminution of sexual function, acromegaly, progressive bitemporal hemianopsia. The hypophysis is usually enlarged, the sella turcica and all the pneumatic cavities of the skull are dilated. Congenital, as well as nervous influences, among others, have been postulated as causes. Some acromegalics (according to Sternberg about one-fifth), belong to the giants, to the pathological class (Langer; p. 1186).

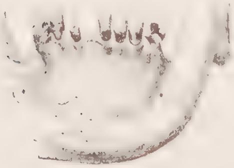


FIG. 551.—Anterior view of the much enlarged lower jaw; diastasis of med. incisors.

Keith, lit., believes the bone changes in acromegaly are parallel to those in the anthrapoid apes and in the Neandertal race.

Generalized hyperplastic periostitis and ostitis represent various processes spread over the entire skeleton, either localized to the bones, or combined with thickenings of the soft parts:

(*a*) Osteoarthropathie hypertrophiante pneumique (Marie; Bamberger), consists of processes observed chiefly in younger individuals and those of middle age, rarely in children and in seniles, as secondary conditions to chronic heart and lung diseases. The nervous system is not involved. Among the heart diseases may be mentioned those accompanied by marked cyanosis, *i.e.*, particularly the congenital heart diseases, and among the lung diseases particularly those with putrid bronchiectasia, putrid bronchitis, fistulous empyemas, phthisis, more rarely lung tumors (Teleky, Weinberger), other suppurative processes in the thorax (Thompson, lit.), etc.; thus, as in the author's experience, a prevertebral abscess in tuberculous vertebral column caries (see also Alamartine, lit.). The changes are always symmetrical and painless, and show gradual differences. The first to be involved, and sometimes the only parts, are the end phalanges of the fingers and toes; the periosteal overgrowths produce thickening and broadening; under the deposit the bone is unchanged or sclerosed, less commonly rarefied (for example, the case of Maresch). Ordinary "drum stick fingers" are usually caused by enlargement of the soft parts, but occasionally are accompanied by periosteal thickenings; the nails lie hour-glass shaped upon the swollen phalanges. For unilateral drum stick fingers in aneurysms of the subclavian arteries, see E. Ebstein, lit. and Bauer. (Lit. by P. Ebstein and Hogler, who speak of acropachia, and Hoffmann.) But drum stick fingers may occur in healthy individuals, occasionally in families (Weber). They may disappear when the causative factor, for example, a pleural empyema, is cured. Braun thinks of removal of a temporary secretory disturbance of the hypophysis, but in individuals suffering from heart and lung diseases, Bamberger found a sclerosis of the cortex and even of the spongy parts of the bones of the extremities, in addition to the ossifying periostitis, while Grafe and Schneider found a more or less extensive rarefaction of the bones. The hands finally become gigantically broadened and thickened, usually asymmetrically, inasmuch as the distal ends of the phalanges become the broadest and thickest parts. In other cases, the shafts of the bones, sometimes merely the distal ends and chiefly those of the forearm and the leg, are covered throughout with flat periosteal deposits. The crest of the ileum may also become thickened. Spindle-shaped protuberances produce important changes in the joints, as observed in severe cases, whereas the cartilage is eroded only in exceptional cases. (The designation osteocarthropathia is thus overdone, and the addition, pneumique, is too narrow; see Kruger and Vas, who speak of acroelephantiasis ossea and mollis.)

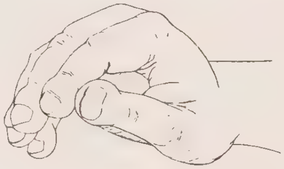


FIG. 552.—Clubbed fingers (drum-stick fingers); ⅓ nat. size.

(*b*) Similar, chiefly ossifying, periostitic changes are observed in syphilis, both congenital (fig. 3, p. 1136), and acquired (p. 1141), and also in chronic icterus (Obermayer, Beuttenmuller, lit.).

The changes in (*a*) and (*b*) are probably results of venous hyperemia in the bones, and possibly also of irritation of toxic substances produced in the bronchial and lung diseases or suppurative processes in the thorax, from which they are absorbed into the tissue fluids; the assumption of toxemia is also permissible in icteric autointoxication and in the conditions of pregnancy resulting in osteophytes (p. 1094), they may certainly be assumed to appear in syphilis (lit. Spieler). Attention may be called to the relatively rare cases of diffuse ossifying periostitis in leukemia (lit. Schlagenhaufer), as well as to the fact, long known (Gies), that phosphorus and arsenic, even in minimal doses, lead to an ossifying periostitis.

Necrosis of the Bones, the Formation of Sequestrae

Necrosis of a Bone is Local Death of a Part.—Local disturbances of nutrition separate the dead part from the living tissue by reactive inflammation with suppuration and by the formation of granulation tissue; when it is thus demarkated, it becomes a sequestrum.

But this is not without exception, for occasionally a transplanted dead bone is not sequestrated, and in chronic osteomyelitis, frost bites (Kleinschmidt, Ribbert, Serra), amputation stumps, the bone is rather necrotic than sequestrated; the dead bone is retained for a time in the body and is slowly substituted by growth from the neighborhood (p. 1082); demarkation occurs inside of the dead part (Axhausen).

Axhausen, who insists upon a sharp differentiation of necrosis and sequestrum, believes that necrosis in fractures is an important causative factor in the formation of the callus, as well as the chief cause for the internal fusion and mortising of the fragments.

Necrosis may be caused by: infectious osteomyelitis and periostitis (p. 1100), which produce the largest majority; thus, for example, in a collection of cases by Trendel, among 1229 osteomyelitic bones, sequestrum formation occurred 1048 times; direct death occurs from chemical or thermic influences (burns, freezing), compressions, comminuted fractures with complete obstruction of nutrition of isolated fragments, from infections, from invasion of ulcers of the soft parts (tuberculous, syphilitic, etc.), in the exanthematous infectious diseases, in typhoid fever (p. 1096), in isolated cases of which a dead part of the upper jaw may be pushed off in a few days (v. Volkmann).

Demarkation occurs because the necrotic part calls forth a rarefying ostitis in the living bone surrounding it, so that the bony trabeculae are destroyed, the union with the neighborhood is removed and finally disappears (figs. 554 and 557). This takes from eight to twelve weeks.

The sequestrum is quite similar to normal bone tissue, but is lighter in weight, almost white in color, dry, very poor in fat. It is therefore quite similar to well macerated healthy bone; in fact, in its macerated condition it cannot be distinguished from normal bone, unless it was already diseased, carious, full of pores or sclerotic at the time of the necrosis (fig. 558-b).

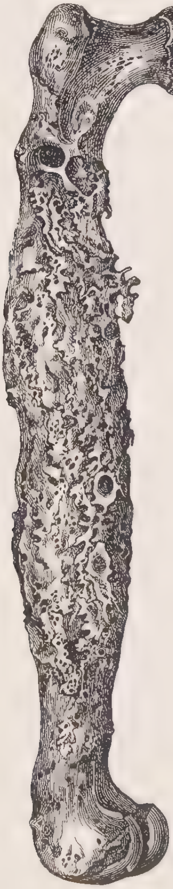


FIG. 553.

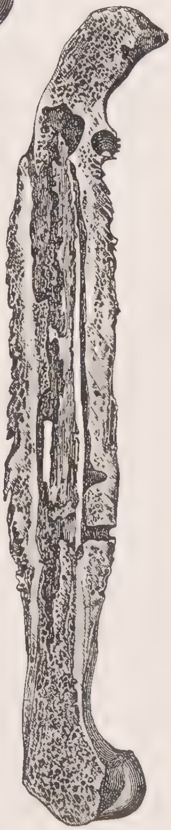


FIG. 554.

FIG. 553.—Total necrosis of diaphysis of femur, with marked exostosis which replaces the necrotic bone. Through exostoses several openings lead to the sequestrum.

FIG. 554.—Same specimen cut lengthwise. (From Billroth's, Allg. Chir.)

If the sequestrum is surrounded by pus, it will not change in years, but if granulations impinge upon the bone, lacunar removal gives it the appearance of having been devoured, or rarefied, raw, or carious; it may finally be brought to total disappearance, though this is uncommon.

The dead part, sequestrated or not, produces and keeps active an osteoplastic inflammation in its neighborhood; the periosteum as well as the marrow and the soft parts of the neighborhood produce a covering of new bone, the so-called bony or capsula sequestralis, which surrounds the

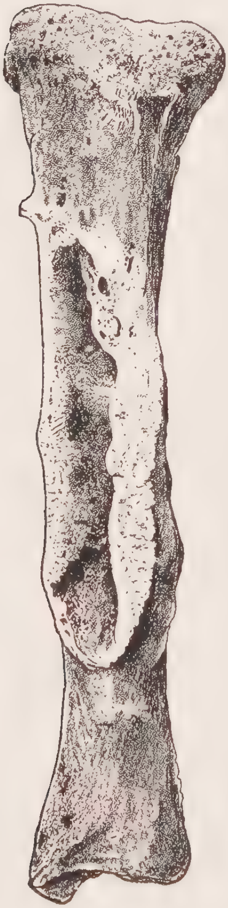


FIG. 555.—Large empty sequestrum capsule, opened at operation, in left diaphysis of tibia with deforming hyperostoses of the whole bone; ½ nat. size.

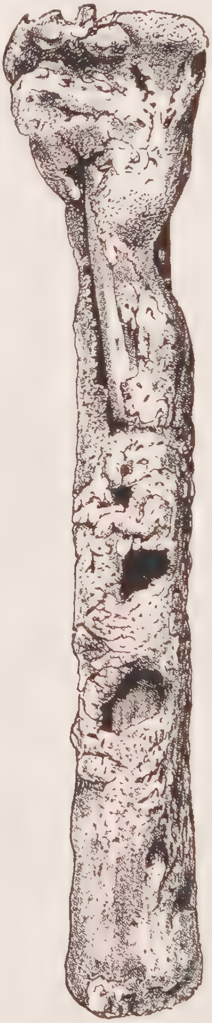
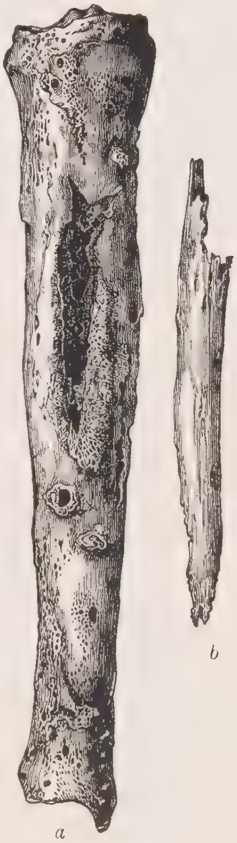


FIG. 556.—Old complete necrosis of tibia with almost complete osseous encapsulation by spongy sclerotic osteophytes. The sequestrum capsule shows numerous cloacae; about ½ nat. size.

dead part like a plaster cast (v. Volkmann). Thus, even when it occurs in the most important case, viz., total necrosis of an entire diaphysis, the continuity of the bone is guaranteed. The dead part is covered externally by periosteum, internally by granulation tissue. In the beginning the new bony tissue is porous, later quite hard; the surface is often irregular like the torn bark of a tree, or like tufa, or angular; in later stages the addition of new bone makes it smoother.

The dead part always has spaces and canals, usually at right angles—bone fistulae or cloacae (fig. 554)—through which the pus reached the surface, and which therefore did not participate in the ossification process. Often the pus reaches the soft parts under the skin through the fistulae and then ruptures externally. The openings on the surface of the skin are usually surrounded by rings of granulation tissue. Other irregular, sometimes very large spaces, in the covering of the sequestrum, shown particularly well in a macerated preparation, are produced by focal periosteal bone formation following focal destruction of the periosteum itself (see the proximal part in fig. 556).

If the necrosis is superficial—necrosis externa s. superficialis—and only partial, a dead layer is cast off, and marrow granulations appear in the depths. If the dead part is larger or the necrosis is total, involving the entire thickness of the bone, very marked sequestrum formation takes place. In central necrosis, the resulting sequestrum, if it remains for a time in the shaft of a long bone leads to marked sclerosis and hypertrophy of the entire bone (figs. 543 and 554).



FIGS. 557–558.—Tibia from a young man after total necrosis of the diaphysis; about 2 years before the tubular sequestrum b had been extracted; the cavity has become almost completely filled with osteophytes; patient died of a carbuncle (Billroth's Allg. Chir.).

Central necroses of the spongy ends of the joints are dangerous because of involvement of the joint itself. Ankylosis may result (see under joints). Partial or total necrosis is commonly seen in the third phalanx in a panaritium periostale, a frequent form of suppurative periostitis, which follows an infected injury of the finger. A disseminated necrosis consists in the simultaneous appearance of numerous smaller necroses in the same bone leading to a number of sequestrae, which then develop many cloacae. According to v. Volkmann, this is probably a concussion necrosis.

The fate of necroses, sequestra, and their neighborhood: healing follows in superficial necroses after the removal, usually spontaneous, of the dead bone. Completely encapsulated sequestrae remain in situ for long times if they are not removed surgically. On the other hand, even very large, but incompletely encapsulated sequestrae may later be extruded by granulation tissue. When the sequestrum is removed, its bed is filled with granulation tissue, which changes to scars or to osteophytes (osteomyelitis ossificans; fig. 557). The final result may be an enormous sclerosis. The fistulae and the cloacae heal. Later resorption produces a new marrow cavity and even the external thickenings may undergo important reduction.

Extensive sequestrotomy and currettage of the bed has led to fatal hemorrhage from the bone vessels in spite of tamponade.

Carcinomas have developed, even though rarely, in old sequestrum beds and fistulous passages, after they had been covered with epidermis. (The author saw this occur in the calcaneum in which a fistula had been present for thirty years; consult case of carcinoma in a thirty-four year old fistula, under the chapter, skin.)

It is rare for the new bone formation to be so poor that pseudarthroses result, for example, in the thigh or the lower jaw. Usually, however, the bones are elastic, even excessively so, and there is not only a thickening (hyperostosis), but also occasionally an elongation of the diseased bone.

So-called phosphorus necrosis is a consequence of a (secondary) suppurative periostitis of the bones of the jaw (particularly the lower jaw), found in workers in match factories; it begins as a rarefaction and frequently, but not necessarily, leads to necrosis. As an industrial disease it usually develops after an individual has worked for a number of years, even ten to twenty, in the factory, and is initiated from local and general (hematogenous) absorption of the fumes of yellow phosphorus acting in a chronically hyperplastic lower jaw. It is seen chiefly in anemic individuals, in those having carious teeth as a predisposing factor, or in those whose gums are injured and infected with spread to the bones (Kocher, Riedel). A suppurative inflammation is caused by the bacteria as manifested when the teeth fall out, and acute periostitic diffuse swelling of the jaw occurs, after which the destructive processes ensue quite rapidly (caries and necrosis). According to the investigations of Wegner—denied by Kissel, but confirmed by Miwa and Stoeltzner and v. Stubenrauch—the long continued administration of small doses of phosphorus (with sufficient calcium, Lehnert), markedly stimulates osteoplastic activities (consult the activity of phosphorus as indicated on p. 1072).

The beginning and the course may vary: (*a*) there is first a suppurative or an ichorous periostitis (v. Vokmann); in these cases Haeckel assumes that a chronic irritation from the phosphorus has already been present producing osteophytes. The pus may rupture externally, and the denuded, partly or totally necrotic lower jaw becomes visible. Around the part, a periostitis ossificans produces a tough covering imitating the shape of the jaw. The pus then lies between the surface of the jaw and the osteophytes. The surrounding parts may later undergo partial or total necrosis; after removal of the sequestrum (duration of a large sequestrum, two to three years), the necrotic jaw may be replaced, of course, without teeth. (*b*) In fulminating cases, the pus lifts the entire periosteum from the bone and its ability to form new bone is completely lost. (*c*) A chronic ossifying periostitis appears first, with the production of osteophytes; this is probably the most frequent form, and according to Thiersch, the rule, but a sclerosing ostitis may appear at the same time. The bone becomes thick, stony hard, and the alveolar canal is narrowed (v. Volkmann). All of this is believed to be a specific local effect of the phosphorus on the jaw, but others believe it is a consequence of the suppuration in the periosteum, (see Kuttner). The next event varies; the process may cease and healing occur, or a suppurative periostitis begins in a carious tooth and leads to partial or total necrosis. The pus remains either between the bone and the osteophyte and separates the old bone from the dead new bone placed upon it, or it lies over the osteophyte. Exfoliation of isolated pieces or sequestration of the entire lower jaw may then occur; or the sclerotic jaw becomes carious and soft before necrosis sets in. The replacement of lifted off periosteum may occur as in (*a*).

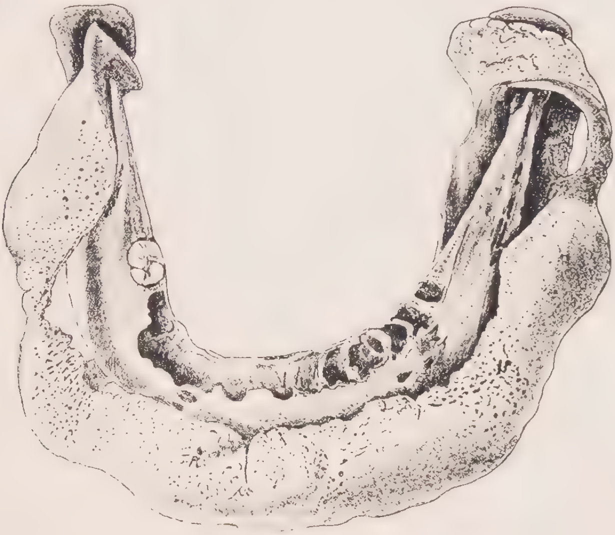


FIG. 559.—Severe phosphorus necrosis (complete necrosis) of lower jaw with immense, stony hard reparatory formation of sequestrum capsule.

Aspiration pneumonia, general infection, or marasmus, leads to death in about one-half of the cases.

Haeckel and Kocher describe a peculiar softness and brittleness of the bones of workers in match factories, which are probably the result of a sclerosis and reduction in the elasticity of the bones, but proper anatomical investigations are lacking in this field. Finally, it is often assumed (Kuttner), that the primary condition caused by the entrance of phosphorus fumes into the blood is a general disease of the bones, recognized by vessel changes and bone apposition in the medulla; this leads to a marked reduction in resistance and the production of a culture medium in which secondary organisms can readily grow.

(Lit. by v. Stubenrauch, Zur Lehre von der Phosphornekrose; see S. kl. V. Nr. 303, 1901, more by Perthes, Teleky; excellent presentation of the clinical picture by Hochenegg.)

Infectious Granulation Tumors

Tuberculosis of the Bones.—Tuberculosis of the bony system is very common. The entrance of the bacilli is often through the blood stream from a focus somewhere else in the body; the tubercles grow internally in the bone, or, more rarely, in the periosteum. An embolic origin is to be assumed particularly for tuberculous ostitis. But infection may be spread from a joint or neighboring parts, usually first into the cartilage or the periosteum.

In those cases of periosteal tuberculosis of the vertebral bodies, in which paratracheal tuberculous lymph nodes are found, but no other tuberculosis in the body, Tendeloo believes that lymphogenous infection from these lymph nodes is the probable mode of origin.

Hematogenous tuberculosis of the bones may be part of a general acute miliary tuberculosis. Then the miliary, or larger, or even conglomerate tubercles in the bone marrow have little significance since the general miliary tuberculosis usually leads to early death. The ordinary forms of bone tuberculosis which run a chronic course are characterized by the development of tuberculous growths with disappearance of the bone (caries tuberculosa).

Bone tuberculosis begins particularly often during youthful years; it often gives the impression of having been directly carried or transferred in intrauterine life. In children, old caseous lymph nodes (bronchial-, neck-, mesenteric) are found in addition to the bone tuberculosis. In adults, there are also pulmonary tuberculosis and tuberculous ulcers of the intestines. Even though many cases of clinically so-called primary bone tuberculosis show old foci which are considered primary at autopsy, it must nevertheless be emphasized that primary tuberculosis of the bone does occur. Thus the author performed an autopsy on a 3½ year old girl with tuberculous caries of the thoracic vertebral column and of the sacrum, with fistulae which had perforated into the rectum; tuberculosis could be found nowhere else. There also was an amyloidosis. In such cases the tubercle bacilli must gain entrance into the body without producing lesions at the portal of entry. From the clinical side, traumata are considered important as predisposing factors for the localization of the infectious organisms (Volkmann and others); but others consider trauma of little moment (six to seven per cent, Wiener). Animal experiments (Schuller, Krause), designed to confirm its importance, have not withstood criticism (Friedrich, Lannelongue and Achard, Honsell and others); a great mass of clinical experience, in spite of lack of confirmation from animals in which the analogy to human conditions is not entirely complete, seems to indicate that trauma may not only be a predisposing factor for the localization, but also is able to stir latent tuberculous foci into activity (Pietrzikowski, lit.). Men, because they are more subject to trauma, are attacked more frequently than women (Cheyne).

Small spongy bones such as the bodies of the vertebrae, the phalanges, metacarpals, calcaneus, etc., and the epiphyses and metaphyses, rarely the shafts of the long bones, are the most frequent sites of tuberculous ostitis.

The typical localization is different from that of (acute) osteomyelitis; suppurative osteomyelitis is situated chiefly in the diaphyses of longer tubular bones. The tuberculous foci may be single or multiple in the same bone, but the latter is not frequent; when present, they are practically always in a large tubular bone in which caseous foci may appear in rapid succession. Occasionally, a number of bones are involved simultaneously, or successively.

The further development of tuberculous bone changes assumes different forms:

In certain cases, invasion by the bacillus is followed by pure tuberculous nodules in the marrow, of a gray color, surrounded by a hyperemic zone; as caseation proceeds, they become yellow. The nodules enlarge by new peripheral eruptions.

But a much more frequent early form consists of gray, or gray red osteomyelitic granulations, which contain scattered typical miliary tubercles (fig. 560). The bacilli are scarce (as in lupus). This is spoken of as a tuberculous granulation focus, or, if diffuse, as a tuberculous infiltrate, or as a fungus. The bone is destroyed where the fungoid granulations are established by a tearing apart of the bone or by partial necrosis depending upon the particular quality, *i.e.*, the fate of the granulation tissue. Occasionally the bone is destroyed by lacunar dissolving as in any other granular ostitis, perhaps without suppuration (caries sicca). But if the granulations undergo caseation or if they are quite atonic and poorly nourished, they lose their ability to destroy bone. Then the trabeculae lying in the caseous tissue merely die; they become necrotic (bone

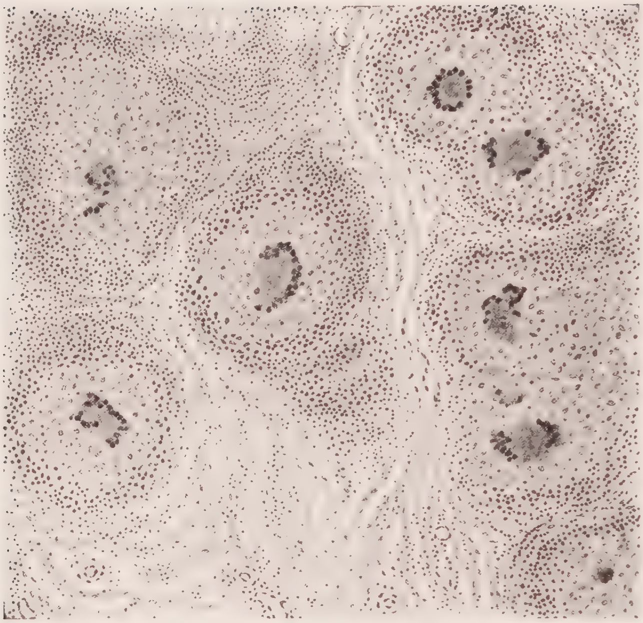


FIG. 560.—Tuberculous granulation tissue from fungus pedis of a 20 year old girl. Epithelioid cell tubercles some conglomerate with Langhan's giant cells and lymphoid infiltration of peripheries. (High power.)

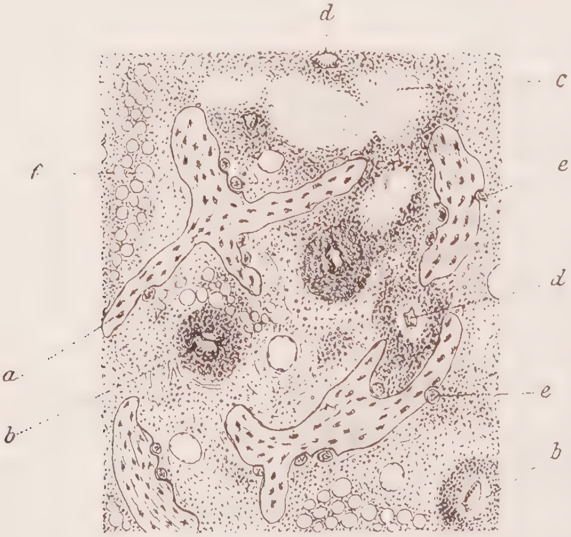


FIG. 561.—Tuberculous caries of a metatarsal bone; a, bone trabeculae; b, tubercle with caseous center, epithelioid and giant cells; c, caseation in tuberculous granulation tissue; d, giant cell in tubercle; e, osteoclasts, some in Howship's lacunae; f, fat-containing bone marrow (yellow); in other places wide delicate veins in bone marrow. (Med. magn.)

sand). Caseation is sometimes very prominent (ostitis or osteomyelitis tuberculosa caseosa), and then even large necrotic pieces of bone are found in the cheesy material, so that the name caries necrotica is often used. Miliary tubercles often appear in the neighborhood. In other cases, a spongy granulation tissue predominates (ostitis and osteomyelitis fungosa), chiefly in well nourished individuals, the caseous form preferring cachectic individuals. Both forms may be combined.

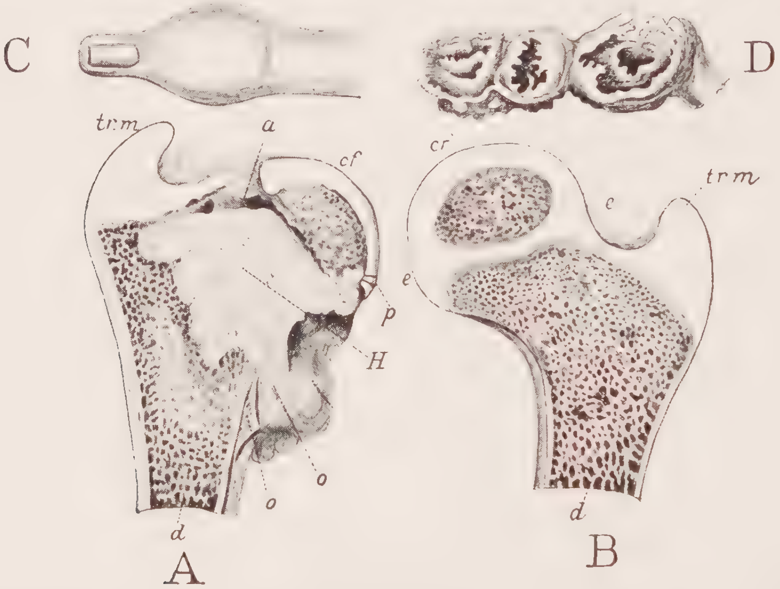
The further course depends upon whether the caseous areas are soft or firm; if the latter, there appear dry, tough, caseous, yellow white foci which occasionally are situated in the spongiosa like a tumor nodule (fig. 562-a).

A caseous focus always contains necrotic bone trabeculae still in communication with the living bone, or separated as a larger sequestrum, or broken up into small particles. The foci may be wedge-shaped with the base directed toward the joint, (anteriorly in the vertebral bodies). This is obviously because of a relationship to the vascular system, a metastatic-embolic affair (Konig), *i.e.*, a sudden occlusion, or an obliterating tuberculous endarteritis with previous dissemination into the area supplied by the vessel (Heile). Such foci have been called tuberculous infarcts (Krause), or tuberculous wedge-shaped foci (Konig). The experiments of W. Muller, Cheyne, Friedlander, and the anatomical investigations of Lexer which pay particular attention to the arterial branches in the bones (p. 1097), lend good support to the view of such an origin; naturally, richly vascular young bones (p. 1097) offer the most fertile field for this process. But such transport of tuberculous emboli occurs, as a rule, only in those who have other serious tuberculous lesions, although they are sometimes primary, in which case the bacilli must have passed through the lungs into the blood stream. When an entire caseous focus is separated, it is by a reactive rarefying ostitis, sometimes developed in a very short time; the borders are a zone of granulations producing much pus or puriform material as they spread peripherally. The sequestrum, surrounded by pus or purulent fluid, is then contained in a so-called tuberculous bone abscess with the peripheral granulation tissue as the abscess membrane. In some cases, cicatricial change in the granulation tissue encapsulates the focus and stimulates sclerosis of the surrounding bony tissue. But this is relatively infrequent because the spongiosa, full of abscesses, breaks under the mechanical strain and allows diffuse spread into the neighborhood.

When the granulation focus has a tendency to rapid caseation and softening, it soon becomes "tuberculous pus," which contains but few bacilli, but many particles of necrotic bone trabeculae, the so-called bone sand. Usually, the process is not true suppuration, but merely a puriform softening, an autolytic liquefaction of tuberculous caseation material.

The ordinary pyogenic organisms are not, as a rule, present in "tuberculous pus" (Krause), unless the focus communicates with the exterior when they readily become secondary invaders.

If the process reaches the periosteum and the surrounding soft parts, or if it ruptures into a joint (p. 1235), the changes are many and severe. Thus the periosteum may be infiltrated by tuberculous granulations, which spread to the neighboring soft parts, and as they undergo caseation they produce the so-called cold abscesses with livid red fistulous passages through the skin, the linings of which are composed of soft tubercle-containing granulation tissue, and the vicinity of which are surrounded by cicatricial tissue.



FIGS. 562–565.—A. Large subarticular, stiff caseous wedge-shaped area H in femur (tuberculous caseous ostitis). Granulations perforated above a, and below broadly to the hip joint (osteal form of coxitis), having destroyed the inner side of neck of femur and spread into adjacent tissue; several periarticular cold abscesses. At o a slight attempt at formation of osteophytes; the epiphyseal line is quite gone. The head of the femur (cf) is in greater part detached from its connection with the neck. At p the articular cartilage is perforated from below; tr.m, greater trochanter; d, shaft, from a 2 year old boy. There was a marked enlargement of caseous bronchial lymph nodes causing dyspnea. Tracheotomy. Death from broncho-pneumonia. B. Frontal section of the healthy left femur of the same child desig. as in A; ee, epiphyseal line; 9/10 nat. size drawn from fresh prep. C. Spina ventosa of the second phalanx of a child 2 years old, after Volkmann. D. Spina ventosa of all three digital phalanges, according to Howship; macerated.

Cold abscesses are composed of thin or perhaps thicker fluid (not green like pus), with but few polymorphonuclear leucocytes, but much bone sand, and occasionally larger sequestrae. The fluid may spread in the interstices between the muscles and tendons and also, but less freely, around the nerves and vessels. The process is less purely mechanical transportation, than an expression of the spread of tubercles, not in the direction of gravity, but, in general, in the direction of least resistance (Loffler). The abscesses coming from a vertebral caries (spondylitic abscesses), corresponding to the site of the process, appear most frequently in the anterior part of the vertebral bodies, particularly in the vertebrae of the thoracic and lumbar regions; the abscess localizes in the cellular tissue anterior and lateral to the vertebral bodies, more rarely anterior and in the median line (fig. 566), usually most frequently in the lower, but occasionally in the upper half of the vertebral column. If the cavity lies in the region of the last cervical and the three upper thoracic vertebrae, it may compress the trachea as illustrated in fig. 566, (Pieniazek). The abscess may be in the form of a fist-sized fluctuating or doughy sac, or a transversely placed double sac, which gradually spreads downward as a broad or narrow fistula on one or both sides of the column. If it reaches the ileo-psoas muscle, it spreads in its sheath which becomes hollowed out to a cavity as big as an arm reaching downward to the inguinal region; indeed, in rare cases it follows the larger vessels and has been known to reach the knee. More rarely, the abscess spreads along this sheath but external to it, whereupon it becomes retroperitoneal, enters the pelvis and perhaps passing through the ischiadic foramen, points in the gluteal

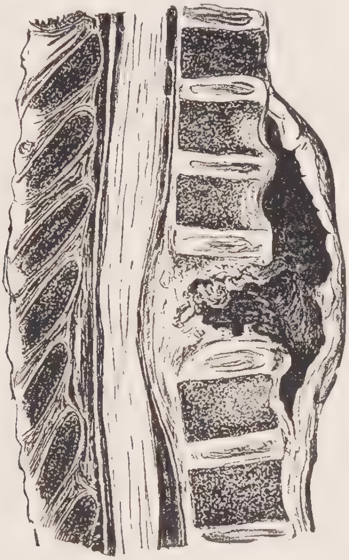


FIG. 566.—Prevertebral abscess in tuberculous caries of the IIIa IV thoracic vertebrae of boy 3 years old with tracheal compression, not relieved by thymectomy (comp. reports of auth. in Cf, Switzerland, No. 16, 1906); 5/6 nat. size.

region. Most frequently a painful swelling appears on the inner surface of the thigh, which, on incision, is found to be a large pocket exuding pus from its ulcerated walls. Spontaneous external rupture usually occurs late. Even the hip joint has been entered by such an abscess. Occasionally, the ileo-psoas muscle becomes a tuberculous caseous cavernous strand of tissue, or becomes infiltrated with bulging abscesses often surrounded by discolored ragged walls; in other cases, it is hollowed out like a gutter with cicatrized walls; in still other cases, the pus disappears almost completely, or becomes thickened into caseous material, the muscle being cicatrized, and discolored gray green (the so-called psoas abscess). But a psoitis may also originate from caries of the pelvis (or sacrum) or of the coccyx; when from the latter the process extends upward. Psoas abscesses have ruptured through the peritoneum into the abdominal cavity or into the descending colon. Caries of the upper cervical vertebrae may produce a retro-pharyngeal abscess (p. 616).

Osteoplastic processes, usually as a periostitis, but also ostitis ossificans, may be combined with the destructive processes. The best known example is the so-called spina ventosa to be described below (figs. 562 to 565-c and d).

Several Especially Important Localizations of Bone Tuberculosis.— It has been stated (p. 1122) that bone tuberculosis prefers spongy bones, particularly the small bones of the hands, the wrists, the vertebrae. In the larger long bones it is particularly the spongy substances of the epiphyses which are involved by the fungoid, granulating, cavitating, caseous, or sequestrum-producing focus, which frequently extends into the joints, particularly the knees and the hips (osteal form of tuberculous arthritis).

A spina ventosa develops in the bones of the fingers or toes, more rarely in the metacarpals or metatarsals, or at the end of a long tubular bone (ulna, humerus), of very young children. In children there is a large artery in the diaphyses of their short tubular bones which favors the lodgement of infectious material; these bones still contain spongy bone instead of a marrow cavity until the fourth year of life. A spina ventosa is a flask-shaped, sometimes hard, sometimes elastic protuberance which usually spares the nail as well as the joint (p. 1126, illust. c and d). In its inner parts there is resorption from tuberculous granulation overgrowth (myelogenous tuberculosis), and the marrow cavity becomes dilated; externally there is a periosteal growth which produces bone or merely incompletely ossified periosteal layers. This relatively benign condition may be multiple, and occasionally runs its course without rupture and suppuration; sometimes, however, fistulae appear; many disappear spontaneously and leave but a small degree of disturbance in growth. When treated surgically, healing may take place with extensive plastic bone replacement (Muller, and lit. by Silbermark). But if the healing granulation tissue shrinks markedly, this, together with the pull of the tendons, reduces the fingers to club-shaped rudiments. The condition has been called of old, padarthrocace. See also spina ventosa under syphilis, p. 1142.

When tuberculosis occurs in the vertebrae, it usually involves a number of vertebral bodies, perhaps four to six or more; the process is only occasionally localized to a single one; the most frequent sites are the lower half of the thoracic and the upper part of the lumbar column, then the middle part of the cervical column. According to Seemann, most cases begin in the first decade. After the twentieth year, tuberculosis of the cervical vertebrae becomes more and more uncommon, and beyond the fiftieth year, it occurs practically only in the lower parts, particularly the transition from cervical to lumbar column. A cortical caries may begin in the anterior parts around the intervertebral discs and remain localized for a long time to the anterior surface, but characterized by tuberculous subperiosteal granulation tissues, and diffuse caseous internal ostitis, central in the vertebral bodies, it may finally destroy the bodies, liga-

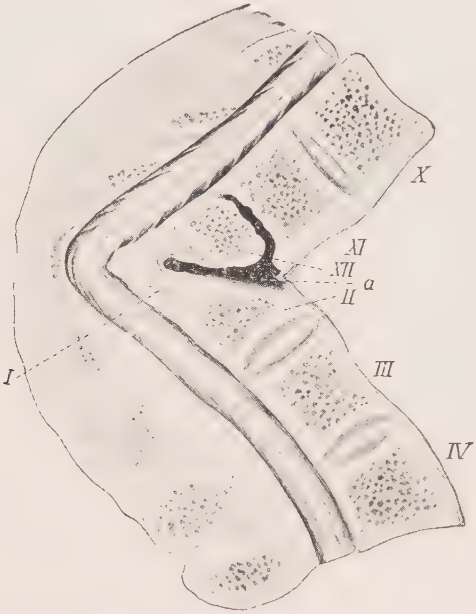


FIG. 567.—Pott's kyphosis; angular kinking due to destruction of the XII thoracic, I and part of II lumbar vertebrae. The I lumbar vertebra is atrophied completely with exception of a small wedge, and with the XII thoracic vertebra is surrounded by soft tissue masses. From the abscess cavity a, into which projects the carious XII thoracic vertebra, bilateral gravitation abscesses spread downward into the psoas which was excavated like a trough to Poupart's lig. From a girl 29 years old who died of ulcerative phthisis and amyloidosis. There were no compression symptoms of the spinal cord; ½ nat. size.

ments and discs so completely, that the upper parts of the vertebral column are no longer supported and hence sink downward. (A third localization according to Wullstein who has related them to blood vessel division, is in the epiphyses.) Finally, the vertebral column is softened, cavitated, broken into pieces, or mechanically crushed and made flat or wedge-shaped. The vertebral column collapses, often helped by a trauma. This is Pott's disease or Pott's kyphosis (figs. 567 and 570), an angular kink of the vertebral column, the angle open anteriorly. The bodies may compress the spinal cord directly, but this type of compression is uncommon. As a rule, it is an extradural cold abscess which narrows the vertebral canal, and thus compresses the cord (so-called compression myelitis or, better, myelomalacia, see under this heading), with subsequent paralyses. The frequency of paralysis and compression increases, according to Seemann, the higher the level of the infection. Rupture into the canal of a focus in the posterior part of a vertebral body may lead to tuberculosis of the dura and tuberculous meningitis, or to an extradural collection of caseous material and bone sequestrae which compress the spinal cord.

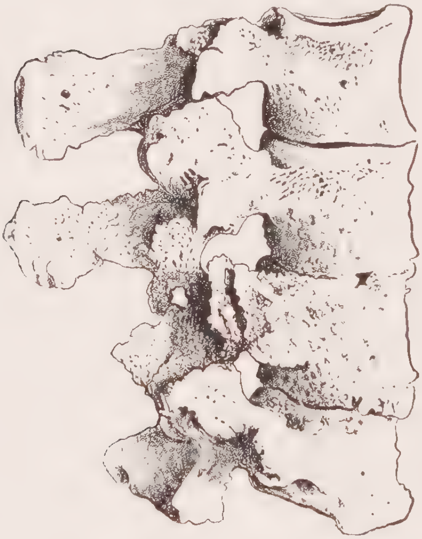


FIG. 568.

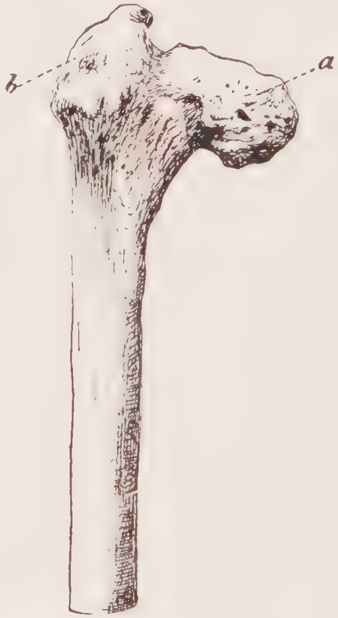


FIG. 569.

FIG. 568.—Tuberculous caries of several lumbar vertebrae with especial participation by transverse and spinous processes; a post vertebral abscess at the posterior cirumference of the spinal canal. Bone bridges have formed across the intervertebral discs of the three lower vertebrae by fusion of supracartilaginous exostoses. Woman of 58, with phthisis and intestinal ulcers; death from perforation peritonitis.

FIG. 569.—Atrophy of the greater part of the head of the femur from tuberculous caries; a, sclerotic healing of stump; b, greater trochanter.

Every experienced pathologist knows of cases in which vertebral tuberculosis remained latent for many years, and then spontaneously led to death after a short course. The author has seen this occur in younger, as well as older, and very old individuals (see also Collins).

In fresh cases the angle still retains a certain amount of motility, but when the caries heals, it is completely and permanently fixed by bone formation, *i.e.*, the kyphosis is fixed; this usually occurs in the course of three or four years. In many cases the kyphosis remains in spite of total disappearance of a number of vertebral bodies. This may occur, for example, when the patient—usually a child—is kept in bed a long while, because of a coincident fungus of the foot or knee, and also because the spinus processes and the transverse processes are still intact. More rarely, the prolongations of the vertebrae, particularly the transverse, are involved (fig. 568); these give rise to postvertebral abscesses. Prevertebral congestive abscesses (p. 1127) are much more frequent, since the caries usually begins anterior in the vertebral column; their frequency increases the lower the level of the tuberculosis (Seemann). A tuberculous caries of the vertebrae may also spread to the ribs, and cold abscesses develop in the peripleural tissue. More frequently, however, rib caries results from tuberculosis of the lungs. A primary tuberculous periostitis may also occur in this situation.

Caries of the Atlas and the Epistropheus.—In many cases vigorous turning or brisk lifting, or bending backward of the neck, causes collapse of the bones and sudden death (respiratory paralysis), in which it is common to find the odontoid process of the epistropheus pressed into the medulla oblongata.

Secondary tuberculosis of the skull is spread relatively often from the petrous bone following tuberculosis of the mucosa of the pharynx. Tuberculosis of the nasal mucous membrane may also lead to secondary tuberculosis of the bones; the same is true of tuberculous inflammation of the external skin (lupus). Primary tuberculosis, on the other hand, is quite rare; in the vault of the skull it occurs more commonly in the frontal and temporal regions, and usually in individuals (especially children), with extensive general tuberculosis. There occur (*a*) a caseous ostitis, often multiple, which leads to rounded perforations—"perforating tuberculosis," v. Volkmann—usually of the posterior part of the temporal bones; (*b*) a periosteal form which leads to abscesses, or to external rupture, but rarely, since the firm galea and the scalp are interposed; on the other hand, tuberculous granulations may penetrate the bone, appear on the dura, the meninges, the sinuses, and lead to meningitis, sinus thrombosis or erosion of a sinus or an artery. A tuberculous granulation may originate in the external periosteal layer of the dura and produce a subsequent caries. The defects are often surrounded by a flat wall of osteophytes in the vitreous table. Tuberculous caries is relatively frequent in the upper jaw, producing fistulae into and through the floor of the orbit.

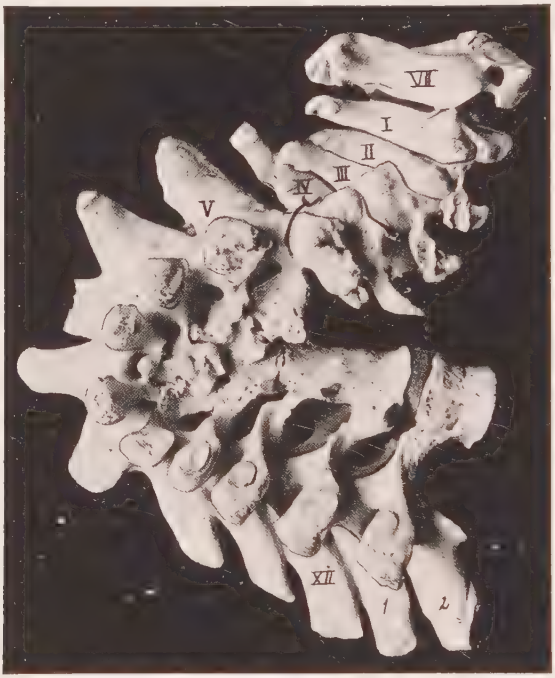


FIG. 570.—Pott's kyphosis of lower thoracic vertebrae fixed in acute angle; VII. 7 cervical; I–XII. 1–12, thoracic; 1 and 2 lumbar vertebrae.

Consequences.—Smaller, or even fairly extensive foci may heal spontaneously, especially in well nourished children, whereas after bone growth is completed, the tendency to heal is gradually lost. A reactive granulating ostitis is produced around the healing focus, and leads either to a scar or to bone production. But fibrous healing is only apparent, because the tubercle bacilli may be retained in the scar, and the old focus can regain its activity, even after many years. On the other hand, even markedly deformed parts, as for example, angular broken vertebral bodies, may be fused together by sclerotic bone masses after removal of the tuberculous process (see fixed Pott's kyphosis).

For the course and the end results of spondylitis tuberculosa, see Kleinmann.

Coxitis, after carious destruction of the larger part of the head of the femur, may occasionally heal by sclerosis and even synostosis of the remnant of the head and the acetabulum (fig. 569).

Bone tuberculosis is rarely the point of origin of distant secondary foci. But in cadavers, particularly older individuals, with bone tuberculosis, extensive tuberculous changes are frequent in other organs such as the lymph nodes, the lungs, intestines, etc. While these other tuberculous changes are often the cause of death, yet in other cases these affections have run their course, and it is the suppuration in the tuberculous bone which leads to amyloidosis and to death. A generalized miliary tuberculosis very rarely originates from a bone.

For purposes of differential diagnosis it might be pointed out that the bones in lymphogranulomatosis, as Askanazy described, may contain yellow foci without bone dissolving, (resembling bone carcinoma); it may also produce fibrous gelatinous deposits in the marrow, and also, as in tuberculous spondylitis, may be accompanied by the formation of cavities.

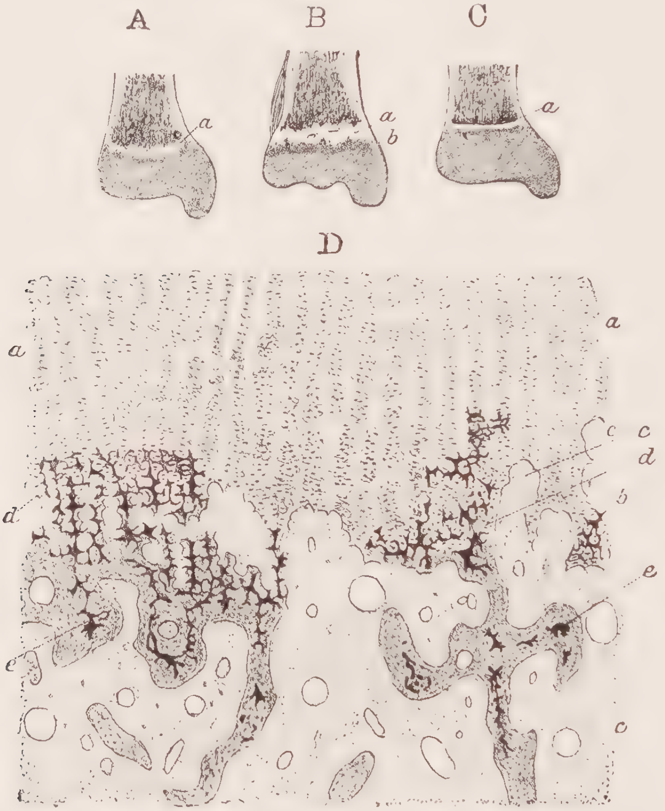
Syphilis of Bones. Congenital Syphilis (see also under skin).—The condition appears from the sixth fetal month onward in the cartilaginous preformed bone, in the form of a so-called osteochondritis syphilitica, as a rule, (Wegner), less frequently, as a periostitis ossificans (p. 1137 and figs. 575 to 577).

Connective tissue preformed bone (parts of the skull), is less frequently attacked by congenital syphilis (p. 1138).

This osteochondritis is extraordinarily important practically. In the first place, it is very frequent; Thomsen found it in 97% of syphilitic fetuses over six months old; (82% of all syphilitic children are prematurely born, Seitz). Secondly, it is possible to identify the condition as a positive symptom of congenital syphilis even in macerated still births (so-called decomposed fetuses), in which other signs of syphilis can no longer be demonstrated such as skin diseases (see under skin), interstitial inflammations of the pancreas, the liver, the lungs, spleen, etc., (see data, p. 462). Recently, spirochetae have been demonstrated in the bones; they invade the growing bone tissue chiefly from the marrow; in the former they often are present in the bone bodies (Schneider, lit.). In general, spirochetae are quite numerous in the organs of macerated fetuses (they increase in number after the death of the fetus).

Since the process is not developed to equal degrees in all parts, and may actually be quite mild, it is advisable to examine many sections of the bones, especially microscopically. As Orth emphasizes, the longer the child lives, the less marked the changes.

The lesions occur at the transition places from metaphysis into epiphysis, particularly of the femur and the lower leg, then the upper and lower arm, then the ribs, more rarely other bones, thus in the crest of the ileum and the shoulder blade (Eug. Fraenkel). The author has seen such pictures, even in otherwise not particularly severe cases. For syphilis of the fetal vertebral column, see Alexander. Wegner recognized that those bones are most intensively infected in which the growth is largest in comparison to their length, and of both epiphyses of the same bone, that which contributes most to the increase in length.



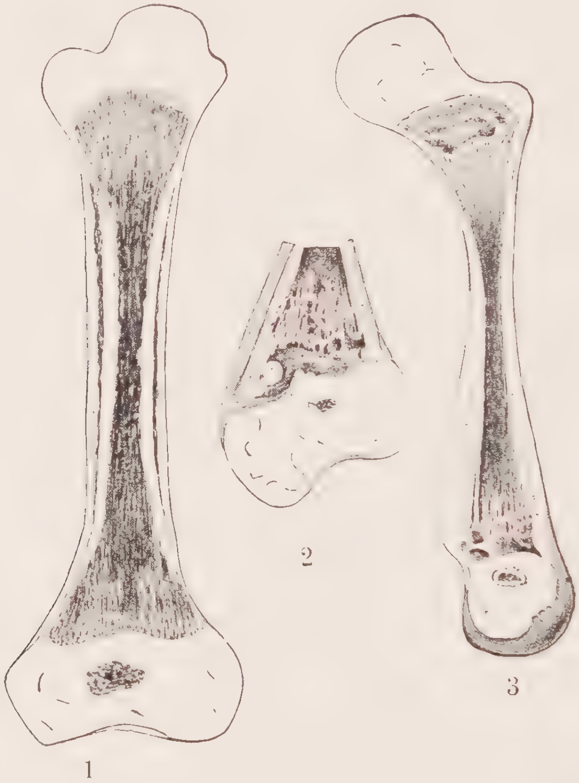
Figs. 571–574.—Syphilitic osteochondritis; A, B, lower end of tibia. Various degrees of change. At a broader irregular bordered zone of calcification; b, broad zone of cartilaginous proliferation. C. Lower end of tibia, normal; the cartilage is dark, bloody-moist. D. Syphilitic osteochondritis (II stage); a, zone of cartilaginous proliferation; b, zone of calcification, quite irregular, interrupted, some calcified areas (calcification lattice) much advanced; c, marrow spaces, wide, advancing quite irregularly toward the cartilage; d, large cell cartilage, its interstitial substance partly calcified; e, remains of calcified cartilage within the sparse shapeless bone structure. Hematoxylin-carmine stain (med. magn.).

Different stages or degrees of osteochondritis may be differentiated. In the first stage, the normal tender, straight, chalky white line representing the zones of calcification (fig. 571-c), is angular, spread out, and yellow (fig. 571-a and b). Occasionally the change is mild, macroscopically, but microscopically there is great irregularity of the broad calcification zones, in which reticulum-like columns of calcified ground substances are especially obvious; calcium-free normal and early calcified situations alternate. The opening of cartilaginous cell columns from the medulla occurs as ordinarily, but the formation of bone is diminished; the functional ability of the osteoblasts is reduced. The subepiphyseal marrow spaces are correspondingly irregular. The bony trabeculae are of unequal thickness, have but few osteoblasts lying upon them, and contain irregular, often very important, rests of broken up calcified cartilage. Very many giant cells appear in the richly cellular marrow. In the second stage the yellow line is much broader, irregularly thick, angular and extended in yellow, tongue-like processes into the bordering epiphysis. Occasionally the zone of cartilaginous growth may swell from overgrowth. (Can be mistaken for rickets.) Microscopically, there are transitions into the granulation tissue type to be described below.

The growth of cartilage may, however, be absolutely lessened (Tschistowitsch). An important differentiation from rickets is the predominance of the calcification in ostitis syphilitica, whereas the calcium salts in rickets are diminished.

In still severer degrees (third stage), a gray yellow, or gray green granulation tissue is forced between the zones of calcification which are now very variable, ofttimes small (fig. 577), or even lacking (fig. 577), or broad and brittle; in the severest cases, the granulations actually break up the continuity of the bony trabeculae, or are liquefied and spread in all directions or are gathered in foci (figs. 576 and 577). M. B. Schmidt has studied the origin of this granulation tissue, and demonstrated its relationship to the canals in the cartilaginous marrow (v. Langer). These latter are physiological structures surrounded by connective tissue prolongations from the perichondral vessels at the border between the diaphysis and the epiphysis. The connective tissue covering is called cartilaginous marrow, and it is from this that the granulation tissue originates. The canals are dilated, by confluence produce irregular spaces and cavities in the calcified cartilage, and these spaces are filled with the growing tissue. Fatty degeneration produces a yellow color in this granulation tissue. The formation of marrow spaces which continue from the diaphysis to the zone of calcification is thus interrupted and hindered. At the same time, yellow, tongue-shaped prolongations of the cartilaginous canals force their way into the bordering epiphysis. In this tissue, called by some merely inflammatory, and by others, true gummatous tissue, (also occurs in the secondary stage but in mild degrees), the bony trabeculae, even in the second stage are extraordinarily irregular, thrown together, without axial or parallel directions; many are thin, others absent, so that the continuity of this layer is very loose near to the diaphyseal and epiphyseal borders (not actually in these borders). This is readily observed on removal of the bones, but may occur in normal bones if they are not carefully removed, *i.e.*, the epiphysis breaks from the shaft;

in normal bones, however, the uniformly granular or warty diaphyseal surface is always cleanly separated from the cartilage, whereas the fracture surface in the growth zones of osteochondritis, because of the calcified cartilaginous masses is irregularly angular, granular, and brittle. In very severe cases the epiphyses separate spontaneously; this should not be mistaken for the separation of epiphyses from decomposition in cadavers, in which the epiphyses are diffusely red from imbibed pigment; various other artefacts may produce the same picture. According to M. B. Schmidt, separation takes place in syphilis because the granulation tissue



FIGS. 575–577.—1. Severe bone changes in congenital syphilis; 1, bone capsule formation of femur by periostitis ossificans and medullization (see p. 1138). Similar changes in tibiae, fibulae, humeri; baby 3 months old with syphilitic psoriasis, slight osteochondritis (also microsc. demonstrated) espec. of ribs; periostitis ossificans of roof of skull. Spleen 56 gms. Fresh spec. The encapsulation was much more obvious after maceration. 2. Gummatous osteomyelitis. Total interruption of endochondral ossification; periostitis ossificans of lower part of r. femur; its length, 9.6 cm.; baby 6 weeks old, with papules, osteochondritis and periostitis and gummatous osteomyelitis of all large tubular bones. Gummatous caries of frontal bone. Spleen 40 gms. 3. Periostitis ossificans; indication of encapsulation; gummatous osteomyelitis; interruption of endochondr. ossification at the lower epiphyseal border; above, very incomplete formation of bone trabeculae. Marked atrophy of old cortical port. L, femur from the same case as 2.

from the cartilaginous marrow canals does not appear at the cost of the bone already built, but where calcification is proceeding; the spaces and interruptions in the ossifying cartilage are formed before the cartilage can become bone. The epiphyses may be separated from a number of bones, but may be reunited, even during intrauterine life, (Eug. Fraenkel saw intrauterine callus formation). This separation of the epiphyses ("décollement," Ranvier), is, as Parrot showed, the cause of the mobility, *i.e.*, the so-called "pseudo-paralysis" of a member (for true birth palsies of the arm, see Froelich, Peltesohn); it is observed particularly at the lower end of the humerus (Hochsinger), or the lower end of the radius, but also in the lower extremities (Eug. Fraenkel, Wegner). The author has seen cases in which the solution of continuity in the humerus was not actually subepiphyseal, but rather below, in the metaphysis (p. 1097); according to Eug. Fraenkel, this is almost the rule; true fractures occur in the bony trabeculae which are first laid down in this situation.

Concerning paraarticular abscesses as complications of severe forms of osteochondritis, see Hochsinger, Kaumheimer.

Osteochondritis seldom produces shortening, but, on the contrary, in most cases the bones become longer; very often, however, healing leaves no trace (Taylor); according to Hochsinger and Eug. Fraenkel, osteochondritis disappears in an astonishingly short time after suitable therapy, while coincident with this disappearance, a periostitis ossificans appears, the dignity of which has not as yet been settled (reparatory process?).

Occasionally, circumscribed, larger, yellow, fatty degenerated, gummatous foci develop in the bone marrow (rare).

Less frequently, periostitis ossificans occurs in the diaphyses, relatively seldom combined with osteochondritic and gummatous changes (figs. 576 and 577); occasionally it occurs in all the large tubular bones. The chief site is the actual diaphysis.

Still more rarely, a peculiar form of periostitis ossificans syphilitica of the tubular bones, particularly the femur, humerus, and tibia produces a lamellated covering of bone separated from the cortex by a mass of marrow, (v. Recklinghausen, fig. 575). This peculiar encapsulation, or shell-like formation is separated from the old cortex which remains intact in typical cases by an increased formation of marrow cavities (medullarization), just as the layers in the covering itself are formed. Parrot believed, in contrast to later experiences, that the change is localized to the lower half of tubular bones; it is laid down in the new bone anlage at a time when the old bone cortex is still compact. But in other cases of periostitis ossificans, the old cortex is partly or entirely resorbed (fig. 577). v. Recklinghausen described this occurrence, among others, in a ten year old girl; osteochondritis could no longer be demonstrated; but in a three months old child it still persisted with the covering; the same occurred in our case (fig. 575). (See also Eug. Fraenkel.)

Syphilitic periostitis, ostitis and pachymeningitis in the skull; and diffuse hyperostosis occasionally occur in congenital syphilis (Virchow, Pommer, lit.). It occurred in the cases in which the lung was riddled with gummata, as illust., fig. 208; slightly raised, gray red, gummatous infiltrates the size of twenty-five cent pieces appeared symmetrically on both sides of the frontal bone.

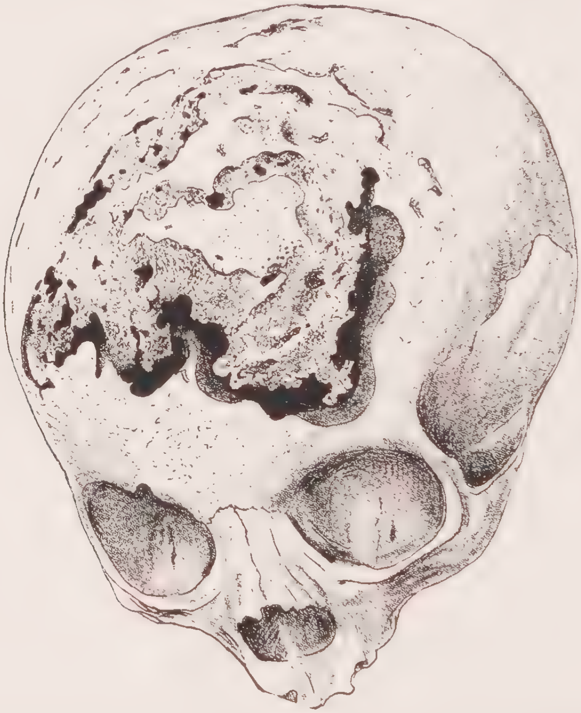


FIG. 578.—Extensive necrosis of anterior part of roof of skull in syphilitic caries, with progressive demarkation of the immense, partly carious sequestrum and multiple perforations. The semicircular demarkation furrows are especially broad and marked in front; hyperostosis of the roof of the skull; superficial dry caries of the rest of it.

Concerning lues "hereditaria," or better, congenita tarda, of the skeleton, see below and p. 1143. For lues congenita tarda of the bones of the face and particularly the jaw, see H. Burkhardt. The lesions which develop in later years of life, not rare in congenital lues, never appear in the form of an osteochondritis.

Acquired Syphilis.—In acquired, so-called constitutional syphilis, bone changes appear, especially in the later, but also in the earlier stages of the disease. But congenital and late congenital syphilis produce quite similar changes which often localize symmetrically, usually during the years of puberty. Bone syphilis is often combined with syphilis of the internal organs. The specific changes consist of: (*a*) destruction of bone by specific gummatous inflammatory products producing caries, and more or less extensive necrosis (caries necrotica); (*b*) new bone formation, particularly periosteal, osteophytic, in part also ostitic. These processes lead to scleroses and hyperostoses, and are also active in the ossifying cicatrization of defects.

The specific gummatous foci appear most frequently in the periosteum, and in the narrower inner spaces of the bones, more rarely in the marrow cavity. The gumma is the lesion of late syphilis.

Fresh periosteal gummatous nodules are seen more frequently by the clinician than the pathologist, as circumscribed, or more or less diffuse, mildly painful, at first, hard, later soft, elastic, pillow-like, swellings reaching the size of an apple, and of the consistency of rubber. On incision, a clear, almost fluid, but viscid mass is emptied; it is poor in cells which are spindle-shaped or rounded. In other cases, the soft cellular growth is so full of round cells that it looks like pus. The growth in syphilis may, however, be quite similar to ordinary granulation tissue, and like this, may become more and more a cicatricial contracting scar tissue. The latter, as is obvious, has nothing particularly characteristic of syphilis. The syphilitic granulations may be recognized more easily if accompanied by vascular changes such as peri- and endarteritis and phlebitis, particularly so when the growing, richly cellular, or the fibrous tissue masses contain yellow caseous foci from fatty degeneration and necrosis. The nuclei in these situations no longer take histological stains. This caseous change of the tissue masses is therefore an important criterion of syphilis.

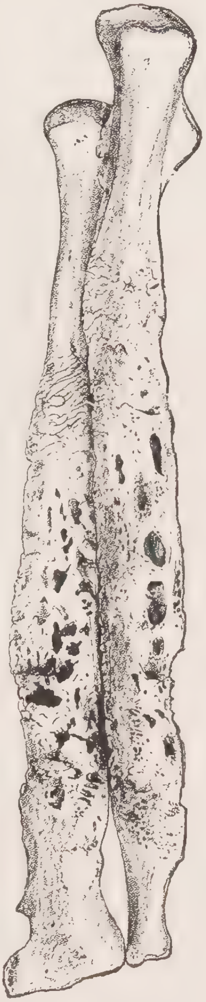


FIG. 579.—Severe necrotizing caries of the bones of the left forearm with formation of very abundant spongy osteophytes in gummatous ostitis and periostitis. The other arm was exactly similar; posterior aspect; ½ nat. size.

This great difficulty of deciding that a tissue overgrowth is syphilitic must be recognized and considered very carefully when surgical measures, *e.g.*, an amputation, depend upon a microscopic diagnosis. The differentiation from sarcoma is often exceedingly difficult. Spirochetes should be hunted (see also under *c*, p. 1102).

The bony tissue is more or less extensively resorbed where the syphilitic growth is established (caries syphilitica or gummosa) without necessarily producing a drop of pus (caries sicca), particularly not in multiple foci of the roof of the skull.

The infiltration may spread into the depths, infiltrate the bones and produce caries, as seen particularly in diffuse gummatous periostitis of the vault of the skull, particularly of the frontal and parietal bones. The gummatous overgrowth follows the vessels which enter the bones from the periosteum. The vessel canals are thus stretched; the openings, small in the beginning, become more and more dilated, so that the bone appears roughly porous and worm-eaten; the confluence of smaller openings produces larger holes, and finally large serpiginous perforating defects. Such defects are often halted at the lambdoidal suture (figs. 578 and 586), but

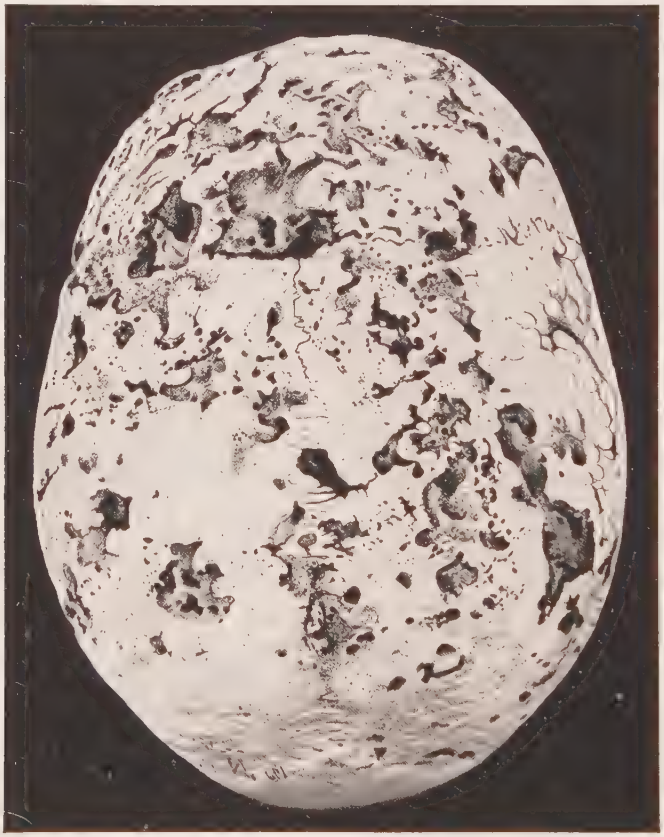


FIG. 580.—Syphilis of roof of skull; chiefly caries, many perforations and marked formation of osteophytes; to right, lumpy large cast-like sclerosed area; its weight, 400 gms.; 5/9 nat. size.

occasionally the entire roof of the skull is involved, the anterior parts more so than the others (fig. 580).

If the cellular overgrowth extends into the dura, it may be followed by gummatous pachymeningitis (see under dura).

A diffuse gummatous periostitis may remain subcutaneous for a long time, and the skin remain quite unchanged, even in the presence of enormous defects in the bony roof of the skull. The unchanged skin merely sinks into the openings. Similar pictures are occasionally seen along the tibia, the clavicles, and the sternum.

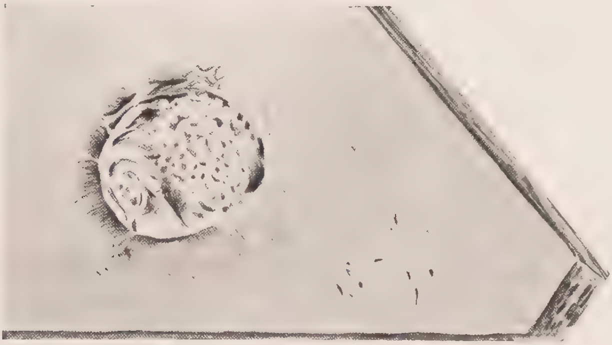


FIG. 581.—Fresh dry syphilitic caries of frontal bone; in the depth of the lesion a bacony gummatous mass; the periphery shows formation of fine bone scars. Woman 60 years old with hyperostosis of calvarium (there were scars in the larynx). Alcohol specimen; nat. size.

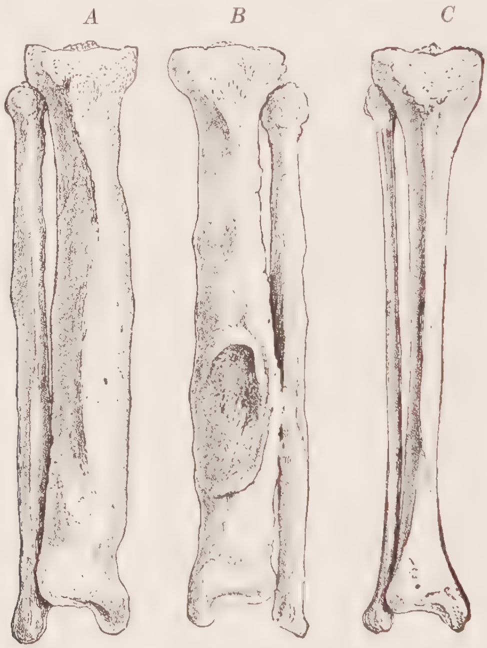
Syphilitic caries often takes on a necrotic character. Smaller, to very large pieces of bone, particularly of the roof of the skull, may be surrounded on all sides by gummatous masses, and thus have their nutrition completely cut off; they become necrotic and sequestrated (fig. 578). The author has seen sequestrae from the roof of the skull as large as a man's hand, which, after removal of the scalp, could be lifted off without further incision. Externally, they are usually roughly worm-eaten; the remainder is sclerotic; complete loosening takes place very slowly, since there are no sound granulations which separate the connections (Wertheim).

If the infiltration ruptures externally, because of increasing thinness of the skin or mechanical insults, suppuration and ichorous exudation result, and the destructive process, particularly the necrosis, is very much hastened. If this occurs in the bones of the skull, meningitis or thrombosis may lead to quick death.

In primary gummatous osteomyelitis there appear circumscribed, often multiple, gummatous nodules followed by central caries and necrosis. The roof of the skull, the phalanges and the sternum are the bones most frequently involved. If the long bones are attacked—a less common condition—local bone brittleness (osteopsathyrosis), and spontaneous fractures are frequently concomitant (p. 1064), while in other cases, the surrounding bony tissue, on the contrary, becomes extraordinarily tough, hard and spindly.

(Lit. concerning ostitis gummosa with spontaneous fractures by Frangenheim.)

Rarefaction of the bones from gummatous granulations may progress also with reactive hyperostosis of the periosteal bone. There thus appear flask-shaped protuberances in the short tubular bones which resemble tuberculosis (see figs. C and D, p. 1126). The bones elongate, particularly the tibia, occasionally with bending "en lame de sabre," a condition which also occurs in late congenital lues; see Spieler, lit., Benazet, lit. (See elongation and deformity of the tibia and the femur under ostitis deformans.) A form known as dactylitis syphilitica is produced by the above mentioned changes in both the acquired syphilis of adults and in congenital syphilis (during the first month of life); in the former it leads to extrusion of necrotic phalanges, invasion of the soft parts with ulcers, fistulae, and occasionally resorption without suppuration; in congenital lues the condition, as a rule, is multiple, and does not lead to ulceration, is painless, and spontaneous regression is possible (Hochsinger). For Roentgen-ray diagnosis, see Krayn.



Figs. 582–584.—A and B, syphilitic, spongy hyperostosis. The thickened leg bones are much lighter than normal. B shows a carious tophus with wall-like edges. Tibia and fibula joined synostotic (there was also syphilis of skull and liver); woman 55 years old. Death of pneumonia. C, normal leg bones for comparison.

General brittleness of the bones may follow syphilitic cachexia without specific changes in their structure.

Syphilomas may regress with the formation of scars (Chiari), during the same time that florid gummatous processes are still in progress in other situations.

Gummatous periostitis and ostitis are often combined with an ossifying periostitis and ostitis, which take care of the bony healing of defects. As a rule, this bone formation occurs at the same time that the destructive gummatous products are being formed; in fact, complete rearrangement of the bone, in the form of simultaneous destructive and constructive processes without softening and suppuration is quite characteristic of syphilis.

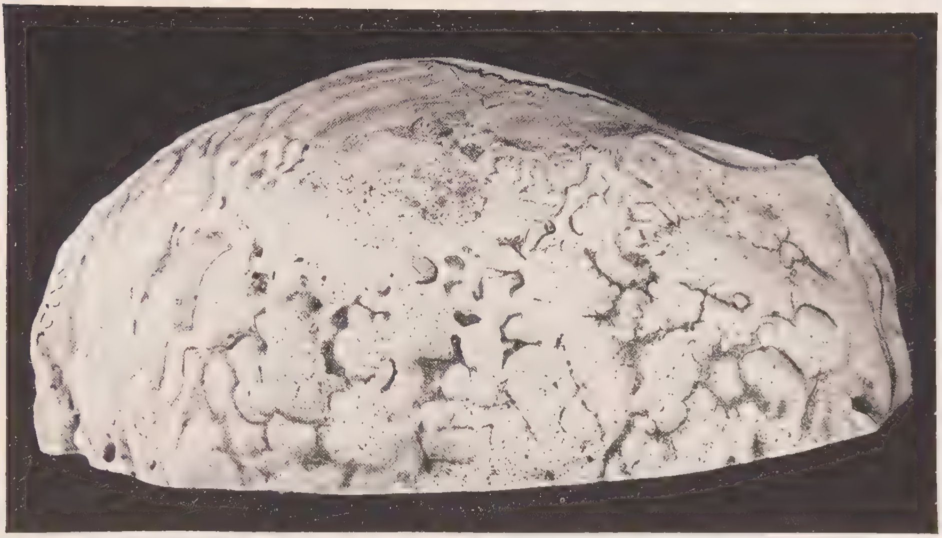


FIG. 585.—Syphilitic sclerosis of roof of skull. The carious lesions mostly fused and closed by new bone formation; only isolated defects; parietal bone averages 1.4 cm. in thickness; to the left, squamous suture; lambdoid suture almost completely fused; 3/5 nat. size.

Thus the surface of the roof of the skull may show innumerable furrows, which lead to rough sequestrae, and at the same time show numerous healed sclerotic depressed situations. The roof of the skull is markedly thickened, perforated in many places, while in other situations there is a thick, stony hard hyperostosis as thick as a finger. Axhausen calls attention to the significance of necrosis of the bones, which is an irritant, and also the object of the internal rearrangement which produces new bone, *i.e.*, diffuse thickenings.

In the healing of very extensive caries of the roof of the skull, the coalescence and covering of the defects may occur from luxuriant bone tissue growth which thickens the skull with finely porous or sclerotic tissue (figs.

580, 585). An osteoplastic inflammation is often established at the base of carious infiltrating foci; if necrosis supervenes, the sequestrae have a porous sclerotic appearance. Even in the neighborhood of defects, the reparatory bone new growth may be quite vigorous; a thick irregular bony wall surrounds the defects.

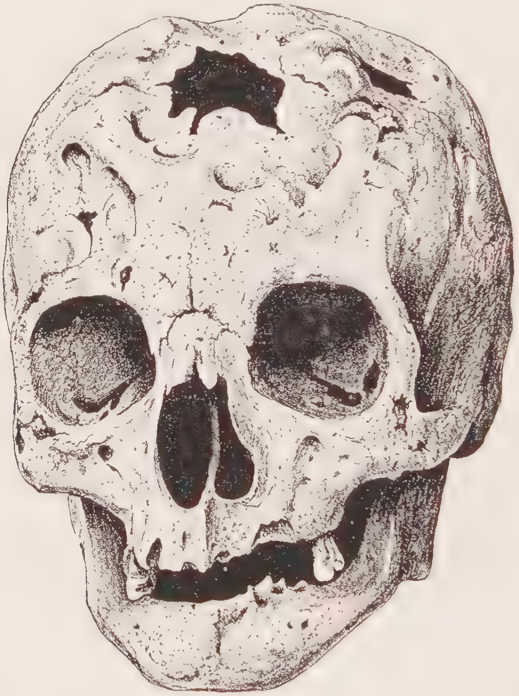


Fig. 586.—Severe older syphilis of skull; necrotic caries partly cicatricially healed; partly progressing. Large hole in frontal bone surrounded by sclerotic bone tissue, outside a wall of sclerotic bone nodules. Smaller hole in l. parietal bone. Deep scars and perforating lesion in frontal bone above r. orbit. Numerous radiating small deep bone scars in frontal bone. Caries and necrosis of malar bones and lower jaw; vomer and turbinates destroyed; perforation of palate.

Occasionally, an osteoplastic periostitis is more independent, *i.e.*, appears without caries. Even in relatively early stages (the secondary stage) of acquired syphilis, small swellings may be found, especially on the fingers. These periostitic processes soon regress, or become bony thickenings. More marked osteoplastic periostitis leads either to quite massive circumscribed hyperostoses, the tophus s. nodus syphiliticus, found particularly in the roof of the skull and the tibia and producing the well known dolores osteocopi, or to the formation of diffuse hyperostoses. The latter appear in the long bones, occasionally, however, in others, but most frequently in the tibiae (figs. 582 and 583).

It is worthy of note that spirochetae may remain latent for long times in the bones and bony bodies, which explains the appearance of local recurrences (Schneider).

An ostitis osteoplastica makes the bones sclerotic, thick, heavy and stony hard. But in other cases, on the contrary, the thickened bones are osteoporotic, very light in weight, and can easily be cut with a heavy scalpel. A rarefying ostitis has appeared in the bone. The surface may be quite smooth (fig. 582-a). Occasionally, the new bone is merely external, but covering the entire skeleton, spread even to the vertebral column (p. 1116); as a skeleton in the collection at Breslau shows, osteophytic protuberances appear everywhere; these are spongy and finely porous at first, but later become dense.

If the gummatous nodules heal on application of suitable therapy, which may occur very quickly, there remain more or less deep furrows produced by a sclerosing ostitis inasmuch as the bones themselves were carious over more or less extensive areas (figs. 585 and 586). These bone scars are occasionally tightly adherent to the skin. Fairly large defects may heal in the form of irregular, deep, smooth or radiating bone scars, or they may be slightly raised above the surface, (fig. 580), but they are nothing else than eburnated sclerotic bone tissue. Very large openings, for example, in the skull, are covered chiefly by scar tissue in their centers, their edges project, and are only partly completed with bone growth.

Relative to the site of syphilitic bone changes, the subject may be summed up, by saying that superficial bony parts are preferred. The roof of the skull, especially the anterior parts, and the tibiae, are involved most frequently; following in order, come the sternum, the palatine process, the bones of the nose, the clavicles, scapulae, humeri, bones of the forearm, etc.

Local trauma in syphilitics is occasionally the predisposing cause for the establishment of bone syphilis. Syphilitic products are said to be favored in their deposition in situations where there was a previous, but healed, bone lesion (Stolper).

Concerning syphilitic vertebral inflammations which appear as a periostitis or a gummatous change with necrosis and the formation of sequestrae even with exostosis formation and nerve root compression, see Ziesche, lit.

(For a recent resume of acquired bone syphilis, see Spillmann.)

Actinomycosis of the Bones.—It is almost exclusively secondary, particularly in the vertebrae and the ribs, from direct extension, from the neighborhood, and, in contrast to tuberculosis, there practically never occurs an independent focus in the interior of one of the vertebrae. It begins, as a rule, as a periostitis, inasmuch as the actinomycotic granulation tissue (p. 466) or an actinomycotic prevertebral chronic phlegmon extends to the periosteum. It usually invades only the peripheral parts of the bone, *i.e.*, the corticalis, and leads to disappearance of this structure by caries, rarely by necrosis, while in the neighborhood, as a rule, a mild osteophyte production occurs (fig. 587).

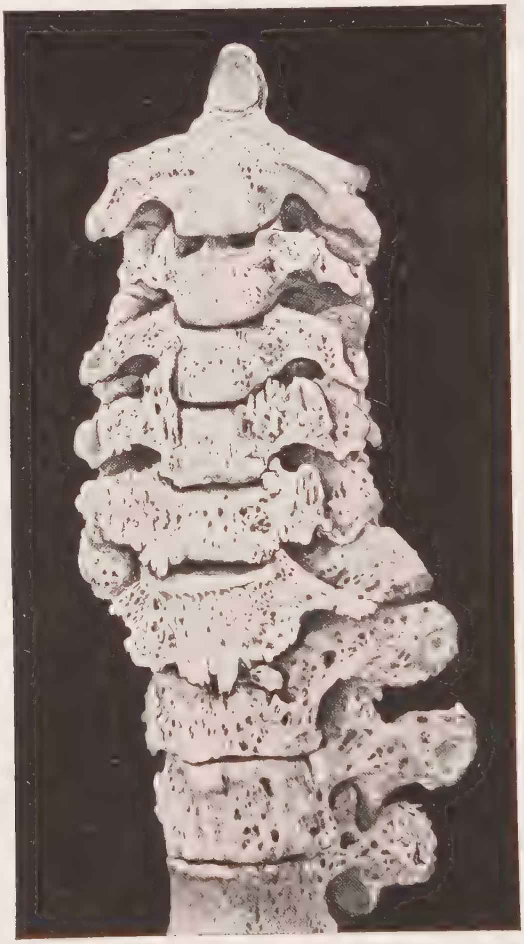


FIG. 587.—Actinomycosis of cervical and upper thoracic spinal column. Superficial caries and formation of osteophytes; anterior view. Above two cervical vertebrae (unfortunately the r. transverse processes of the three thoracic vertebrae were sawed off). Field laborer. There was actinomycosis of the deep cervical tissues and both lung apices.

Usually the process which spreads over rather large stretches in the vertebral column and the ribs, remains permanently superficial, *i.e.*, peri- and parosteal. It is only rarely that actinomycotic granulation tissue extends deeply into the body of a vertebrum (the lumbar vertebrae in ileo-cecal actinomycosis); the picture is then similar to tuberculous caries, and the vertebral column may collapse (Shiota). Often, the destructive process spreads over a long course of time from one bone to another without much suppuration.

An actinomycosis of the skin may invade the bones of an extremity (Tusini; see madura foot under skin). Concerning actinomycosis of the jaw, see p. 557.

By way of the blood stream, bone metastases have been observed in the femur coming from the lungs (Wrede), but few cases have been recorded. There also occurs a primary actinomycosis of the bones (*c*), but it is very rare (Gougerot and Caravin, lit., Keppler, lit.).

Appendix.—In addition to actinomycosis, there also occur the relatively rare human mycoses such as blastomycosis (see under skin), sporotrichosis (see under skin), and hemisporosis (see under skin), producing ostitic, osteo-periostitic and osteo-arthritic processes (concerning the latter, see Sorrel and Verdun), even leading to spontaneous fractures (Zeiliger). In blastomycosis, the growths appear like sarcoma; after softening of hemisporodic abscesses, the osteo- and periostitis may be similar to syphilitic or tuberculous processes, and without culture may readily be mistaken. (Lit. by Gougerot and Caravin.) For experimental sporotrichosis of the bone, and extensive lit., see Bolognesi. See also lit. in appendix.

Leprosy of the Bones.—(See also under skin.) Bacillus-containing leprous nodules appear in the bone marrow and infiltrate the periosteum (Sawtschenko); they are often diagnosable macroscopically (see Sudakewitsch; more details by Hirschberg and Biehler). In their growth, the foci produce caries; a slowly progressing total subcutaneous disappearance of the bone may occur which may simulate actual mutilations. The serious changes which are designated lepra mutilans and which consist of the extrusion of entire members (particularly the phalanges), are, on the other hand, not specific leprous bone diseases, but a result of the anesthesia gradually produced in the type of leprosy called lepra nervorum. The insensitive members are subject to injuries and infections with pyogenic organisms. If this process extends into the depths, the bare bony parts undergo necrosis as in a panaritium periostale.

Harbitz showed that a small number of cases appearing like lepra mutilans are dependent on a peculiar change, recognized by Heiberg, and described by Hirschberg and Biehler, in the nerves as a tropho-neurotic atrophy, which involves the bones. All of the nerves, motor, sensory as well as vasomotor, but not the hypothetical specific trophic nerve fibers, are involved; these normally influence the nutrition of the tissues. Isolated, particularly peripheral, bones of the hands and feet, may finally disappear completely, or undergo concentric atrophy, become short and pointed, sheath-like, or flat. (Interesting illustrations and lit. by Harbitz.)

Disturbances in the Growth and the Development of the Bones

Normal Bone Development.—The formation of bone occurs not only in the embryo, but also after birth until the end of the growth period, (twentieth to twenty-seventh year). It occurs both from the cartilage and the cambium layer, *i.e.*, the osteogenetic internal periosteal layer. Thus we have enchondral and periosteal ossification.

There are differentiated: membranous bone (chiefly roof of the skull—see Thoma concerning its growth in the fetus,—bones of the face, lower jaw with the exception of the angle), and cartilaginous preformed bone. Since, however, cartilaginous masses are found also in the flat bones (see Bonnet, Minot, Gaupp), this sharp differentiation is somewhat obscured.

Intramembranous ossification proceeds by the appearance of bone nuclei—flat bone plates—surrounded on all sides by connective tissue. Two methods prevail: isolated connective tissue bundles undergo calcification and these are applied to osteoblastic bones, or small groups of osteoblasts which come from the embryonal connective tissue cells, without further ado, secrete calcifying substances which become the points of origin for the development of more bony trabeculae (Stoehr). The connective tissue lying upon these plates is called periosteum. From these points of ossification, enlargement takes place in the flat plane, *i.e.*, bone is laid down along the edges and margins (flat growth), while the growth in thickness occurs, by the application of layers of new bone on the external and internal surfaces. The external layers are compact, while between them is found the spongy bony substance, or the diploe.

The cartilaginous preformed bones (the so-called replacement bone) originate primarily from a membranous anlage, first become cartilage and then bone, *i.e.*, the connective tissue membrane is first perichondrium and then periosteum. In the cartilaginous pre-stage of the skeleton, these prepare isolated particles of solid cartilage without vessels and covered by periosteum (perichondrium). Canals then appear in the cartilage, inasmuch as the vessels enter through openings like worm holes; calcium is soon deposited in the neighborhood of these canals. The cartilage close to the canals is then dissolved, so that the cartilaginous canals become irregular in form as the so-called primary marrow cavities. Their contents, the marrow, consist of connective tissue with blood vessels and osteoblasts, all coming from the periosteum, *i.e.*, perichondrium. The marrow therefore corresponds to the richly cellular inner periosteal layer. The osteoblasts are grouped as a layer on the trabeculae of the calcified cartilage where they produce bone substance, inasmuch as they surround the calcified cartilaginous trabeculae with sheaths and coverings of bone. These strands of calcified cartilage (for example, fig. 599), later disappear when the surrounding covering of bone itself is removed by resorption, *i.e.*, apposition for functional demands. The author, however, has seen them retained in extraordinary numbers in a 17 year old youth. Then in the further deposit of bone, as Pommer emphasizes, there appears a provisional osteoid zone (physiological osteoid), which lies upon the calcified young bony substance. (See also Wieland, and p. 1153.) The calcified bony substance gradually disappears again, while the formation of spongy bone keeps pace. (For more histological details, see Dibbelt.)

In the long tubular bones (humerus, femur, tibia, etc.), the deposit of bony tissue begins from the periosteum or perichondrium in the middle diaphysis, so that the cartilaginous shaft is surrounded by a bony mantle which is thickest in its middle. But the cartilaginous tissue grows at both ends of the shaft and serves for elongation as well as for thickening. In the middle of the diaphysis, however, the enclosed cartilage remains quiescent in its growth, because it becomes calcified. The periosteal or, as it is also called, perichondral bony sheaths, take on the form of two funnels with their narrow ends united in the middle of the diaphysis. The sheath at first shows reticular bone, containing numerous Sharpey's fibers; after previous partial resorption, the trabeculae of lamellated bone are then laid down, and produce Haversian canals around the blood vessels; these also still enclose many connective tissue fibers which reveal their origin from a connective tissue matrix. Then the cartilaginous masses filling the funnels are reconstructed by the ingrowth of connective tissue bands (with osteoblasts) and blood vessels from the periosteal bony sheath, and filled out with spongy bone (enchondral bone), by a method similar to that described under (*b*). This enchondral bone is also of provisional character; it is dissolved by the marrow to produce marrow cavities. At birth, all primary enchondral bones have disappeared from absorption from the centers of the diaphyses. But at the ends of the diaphyses, as long as bone growth continues, there is a continuous progression of the enchondral construction process. There remains a flat piece of cartilage, the so-called intermediary cartilage between the diaphysis and the epiphysis, the epiphyseal junction, until the growth in length of the bone has been completed; through the intermediation of this mass of cartilage, young bone appears. By this means, the cartilage is prepared for the entrance of the growing marrow cavity, from which new bone is laid down. Without cartilaginous discs, there is no invasion of marrow cavities, no bone apposition, and thus no growth in length; the latter ceases when cartilaginous growth ceases, which is probably influenced to some extent by the sex glands; if this influence is removed as in castration, the cartilage grows far beyond the normal time and there results a type of giantism (see Erdheim). Ossification is evidenced by a plainly visible straight line at the border of the epiphysis and the diaphysis. The periosteal bone continues to produce new layers, and the older trabeculae increase in strength. Thus fine canals replace the spaces between the trabeculae (Haversian canals), and the thickness of the bone is increased. Some of this bone is also used for marrow cavities and spongiosa, because so much bony tissue is resorbed from the Haversian canals that only the thin trabeculae of spongiosa remain standing. In the compact corticalis, on the other hand, the canals remain narrower, the trabeculae are close together. Later, ossification centers appear also in the epiphyses, as the so-called epiphyseal nuclei. The process also occurs similarly, *i.e.*, entrance of vessels from the cartilaginous surface, and from the diaphysis through the junction cartilage (Bidder), the deposition of calcium, the surrounding of calcified cartilaginous trabeculae by osteoblasts from the marrow and the deposit of bone by these. Endochondral ossification then proceeds from this nucleus, spreads radially, and gradually occupies the epiphysis.

Sometime before birth, the exact time varies widely, but in the seventh month, a bony nucleus is laid down in the distal (lower) epiphysis of the femur, a fact which is often looked upon as indicating that a child is mature (40 weeks old, or 10 months of pregnancy, 280 days), and therefore of alleged medico-legal interest. This nucleus in 90% to 95% of mature births (50 cms. long), is two to five, or as the author has seen, even eight millimeters wide, but may be entirely lacking in mature newborns as known for a long time (Hartmann-Luschka). In estimating the maturity of a child, this focus of ossification is therefore of limited value (Nobiling).

The layers of cartilage close to the joint remain permanently as the joint cartilage; even during the period of growth, this produces very little bone relative to that formed in the growth of the diaphyses, but even into great age, some endochondral ossification can be demonstrated here and there in this cartilage (Fromme).

These three phases of enchondral ossification can best be seen in longitudinal sections of a growing tubular bone, *i.e.*, 1. the growth of cartilage, 2. the destruction of cartilage, 3. the construction of bone. Where the epiphysis and the diaphysis meet, there are two macroscopic zones, that of growth of cartilage is bluish and transparent; between it and the bone is the yellow white linear zone of calcification (illust. C, p. 1134).

The border between the cartilage and the bone shows six microscopic zones (p. 1156, fig. II). (1) The external layer beyond the resting cartilage (fig. II-a), the zone of beginning growth (fig. II-b). The cells are increased in number, without particular arrangement, many are grouped in a capsule. (2) Zone of columns, or cartilage cell columns; the cells are flat (fig. II-c). (3) The zone of the hypertrophic cartilaginous cells, (fig. II-d); the flat cells become vesicular. Some parts of this zone show deposition of calcium in the cartilaginous ground substance. (4) The zone of calcification (fig. II-e), is the macroscopically visible, yellow white, straight calcium line. Into this layer the marrow sends buds of vessels which soften the cartilage, which is (5) the zone of the primary marrow spaces (fig. II-f). In the next layer, the actual ossification is found with osteoblasts from the marrow tissue. (6) Zone of enchondral ossification (*g*) (fig. VI, p. 1060).

Concerning the more detailed structure of the cartilage of the ribs in childhood, (basophile interfibrillar ground substance), see Pommer, lit. [For systemic and sex determinants of bone growth see Hammet F. S., Biolog. Bull., 50: 61: 1926.—*Translator.*]

Rickets

This disease was first described accurately by Glisson (1650) in the seventeenth century in England, but was probably known much earlier by W. Ebstein and others. Rickets is a constitutional anomaly of all the bones, the most characteristic feature of which is paucity in calcium, which is the underlying cause of all the skeletal changes. The bones become soft. Rickets is chiefly a disease of the first period of growth, *i.e.*, the first and second years of life, but may extend into the third year, and in rare cases even into the tenth year of life, while it has been reported as late as the twentieth year (rachitis tarda, see pp. 1166 and 1072).

The question of whether rickets can be present at birth is answered in opposite terms. The author, Tschistowitsch, Escher, Wieland, (lit.), Schmorl and others, do not believe that rickets occurs at birth; according to Wieland, there is also no latent congenital rickets, and Stalfors confirmed this idea in the calf. By way of contrast, Kassowitz (lit.), who in earlier studies called many "cartilaginous disturbances" congenital rickets, but erroneously so, has again stated that congenital rickets does occur. These opinions, therefore, are diametrically opposed. The contradictory investigations concerning the soft skull (p. 1164, lit.), however, still allow for the possibility that there does occur a congenital rickets (Schloss).

Various grades, lighter and severe cases can be differentiated. The disturbance in nutrition at the basis of rickets does not allow sufficient calcium salts to be deposited in the cartilage of the growth zones, and in the newly formed bony tissue (Pommer, Schmorl); there is an overproduction of osteoplastic tissue (periosteum, cartilage, marrow tissue or endosteum), which produces incomplete bone, *i.e.*, non-calcium containing osteoid tissue inhibited from taking up calcium. The osteoclastic resorption processes in the skeleton, as a rule, do not increase beyond that of the normal, nor is the specific bone marrow involved in the process.

In individual cases, the changes sometimes take one direction and sometimes another, the density and the mass of the newly formed bone varies considerably, and there are huge variations in the macroscopic pictures. v. Recklinghausen differentiates (*a*) the porotic, (*b*) the hyperplastic porotic, and (*c*) the hypoplastic porotic forms.

Osteoid tissue, (non-calcium containing bone), comes from the periosteum and the marrow (endosteum), or even from metaplasia of cartilage. The fibrous marrow, remarkable in many parts of the skeleton, (so-called "fibrous osteomyelitis"), is rich in stellate and spindle cells and vessels, but poor in myeloid cells; osteoid trabeculae may appear by direct reconstruction from this marrow tissue (*i.e.*, from thickening of the endosteum), or from flat, spindle-shaped or epithelial-like osteoblasts, as in a callus, but naturally in less amounts. These osteoid trabeculae have a non-lamellated, reticulated, or fibrillary ground substance, although some are lamellated, and contain plump bone cells in irregular distribution. Focal islands of cartilage may also be formed. The above mentioned fibrous osteomyelitis is, however, not always present at the beginning; the marrow is not changed except for a mild decrease in the myeloid cells; the change occurs later (Schmorl), just as the overbalanced osteoid tissue production is called forth by the entire sum of the mechanical, static, and dynamic effects and irritations, which are suffered by the soft rachitic skeleton (Oehme). The osteoid substance is laid down in the inner bony trabeculae previously present; in severe degrees a picture is developed similar to that of a myeloid callus, namely, a dense, finely porous spongiosa, and as in fig. 588, confined not to the metaphyseal parts, but continuing until the marrow cavities of the entire diaphysis are almost completely filled. In other cases, the thickening is external and the osteoid tissue comes from the periosteum (so-called "periostitis rachitica"), with preference for certain areas. These osteoid masses produce thick coverings like a periosteal callus (fig. 589, IV), or plainly divisible layers, as in the long tubular bones, or very richly vascular, delicate, spongy, or creamy periosteal overgrowths (osteophytes); in the reticulated bones the trabeculae are directed at right angles to the bone surface (fig. 589, V). These osteophytes are differentiated from an ordinary bone overgrowth which becomes sclerotic, by the longer duration of their soft cuttable stage, and by their incomplete, often laminated, calcification. This formation of osteophytes is looked upon as a reparatory process, a sort of callus formation, and is found everywhere, where the lamellated bone has disappeared, become bendable, and brittle. The most delicate osteophytes are seen on the external layer of the roof of the skull. If an attempt is made to peel the thickened periosteum off a long bone, larger pieces of porous bony tissue come with it.

As Pommer first emphasized, and Stoeltzner and particularly Schmorl confirmed, the lining of the inner surfaces, and the covering of surfaces of the various parts of the skeleton and the bony trabeculae with osteoid columns, in amounts far above the normal (osteoblasts!), are the most important anatomical characteristics of rickets; they involve all parts of the skeleton, and are found constantly from the very beginning in all types or degrees of the disease, even in those in which macroscopic changes cannot be found (Schmorl). Seams, *i.e.*, lack of calcification in the newly formed bony tissue, are found also in the milder cases, in which the enchondral changes in the layer of the hypertrophic cartilaginous cells begin as "defective calcification zones" (p. 1158), but only in rapidly growing bones (ribs, lower end of the femur, ends of the tibiae and fibulae, upper end of the humerus, lower end of the radius and ulna); in very mild cases, they are completely lacking.

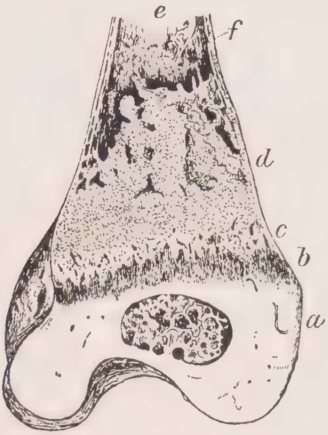


FIG. 588.—Femur of a child 2½ years old with severe rickets. Frontal section of lower part; anterior half. Very marked formation of finely porous osteoid (spongioid) reaching into the medullary cavity; a, lower epiphysis, normal cartilage with bone nucleus; b, soft zone of cartilaginous proliferation, swollen and spotted blue red; c, zone in which vessels and marrow spaces with enchondral osteoid tissue advance into the soft cartilage; d, osteoid tissue in metaphysis and reaching into 1, the medullary cavity which is otherwise wide with but little spongiosa; f, thinned atrophic compact bone surrounded by osteoid periosteal layer; nat. size.

By a modification of Schmorl's thionin staining, v. Recklinghausen demonstrated changes in the osteoid zones of the bony trabeculae of rachitic bones, which he believed were liquefactive processes. These red staining, so-called "territories," are small, rounded spots in the positions of isolated destroyed bony bodies, and larger complexes representing map-like figures, with swollen stripes and columns; these surround the perforating vascular canals with sheaths, which are striped at right angles. v. Recklinghausen is of the opinion that the osteoid tissue is dissolved, which leaves the reticular substance, showing the above mentioned stripes. This dissolving process leaves room for the entrance of spindle and round cell-containing marrow tissue.

According to the older opinions, the healing of rickets takes place from calcification and perhaps sclerosis of the tissue which remained without calcium; if a remission occurs during the course of the disease, the uncalcified bony tissue is calcified (p. 1159); later, however, new osteoid columns appear. According to v. Recklinghausen, most of the rachitic osteoid has no power to fix mineral salts; these osteoid types are: 1. normally formed, but free of calcium, 2. pathologically new formed, 3. osteoid from old bone by halisteresis; before healing can take place, the pathologically produced osteoid must first be removed and replaced by new. Schloss states that this hypothesis explains the negative results of calcium therapy.

In those cases accompanied by osteomalacia, a picture somewhat similar to ostitis deformans may be produced in the skull (p. 1108; v. Recklinghausen). The author has seen many such specimens with pumice-stone thickening, chiefly of the anterior part of the skull (to 15 mm.); in a 2 year old boy, the frontal and coronary and part of the sagittal sutures were prematurely synostotic, while the posterior part of the skull showed translucent depressed areas, while the large fontanel remained wide open.

Vigorous resorptive processes occur chiefly by lacunar resorption, but probably also by halisteresis. This is evidenced by wider marrow spaces in the ossification region at the border of the cartilage and bone. The tubular bones become more and more osteoporotic by resorption of the trabeculae of the spongiosa and the compacta. The flat bones of the skull and also the corticalis of other bones are occasionally thinned to a layer of osteoid or even to the bone membrane. Thus a large part of the skeleton is reabsorbed. These processes, however, must not be overemphasized. Kassowitz indeed believed that the chief cause of rickets was "increased" bone resorption, but against this view, growing bone is subject to quite vigorous physiological resorption, the amount of which is not overstepped in typical or ordinary rickets (Pommer, Schmorl). That which is entirely different from normal is the replacement of the resorbed bone by an incompletely calcified tissue (osteoid), even in greater amounts. Only in rare prolonged cases does resorption overbalance apposition so that an osteoporosis is produced (Stoeltzner).

Cases do occur, however, of "rickets with osteomalacia," which are better called severe rickets with uncalcified new formation and halisteresis, (M. B. Schmidt), in contrast to ordinary rickets (with uncalcified new formation), in which v. Recklinghausen found many reticulum figures, and vascular stripes indicating important halisteritic bone disappearance which may occur over extensive areas of newly formed, as well as old bone. It is desirable, therefore, to examine the osteoid tissue with the view of discovering what was newly formed and what was decalcified; for this purpose Dyrenfurth recommends the staining method of Goetsch. (Looser, who believes that rickets and osteomalacia are identical, disputes the occurrence of halisteresis.) The cortex becomes porous and soft, the marrow cavity, in which osteoid tissue may be developed, is uncommonly wide. The elasticity of the bones is similar to that of infantile osteomalacia, but there are no changes in the cartilage in the latter; the disturbances in enchondral ossification of rickets are the most important differential points between it and the classical osteomalacia of the adult in which these changes are lacking.

The Metaplasia of Cartilage into Osteoid.—Whereas the cartilage at the normal epiphyseal border is but a connecting link between inorganic and organic substances, *i.e.*, it makes way soon after the taking up of calcium salts for the marrow spaces from which the bones are first produced (neoplastic), in rachitis the cartilage ground substance frequently undergoes metaplasia into osteoid (chondroosteoid). The cartilage cells become smaller and change directly into bone cells. The ground substance becomes bone ground substance. This reconstruction may attain considerable extent at the epiphyseal borders.

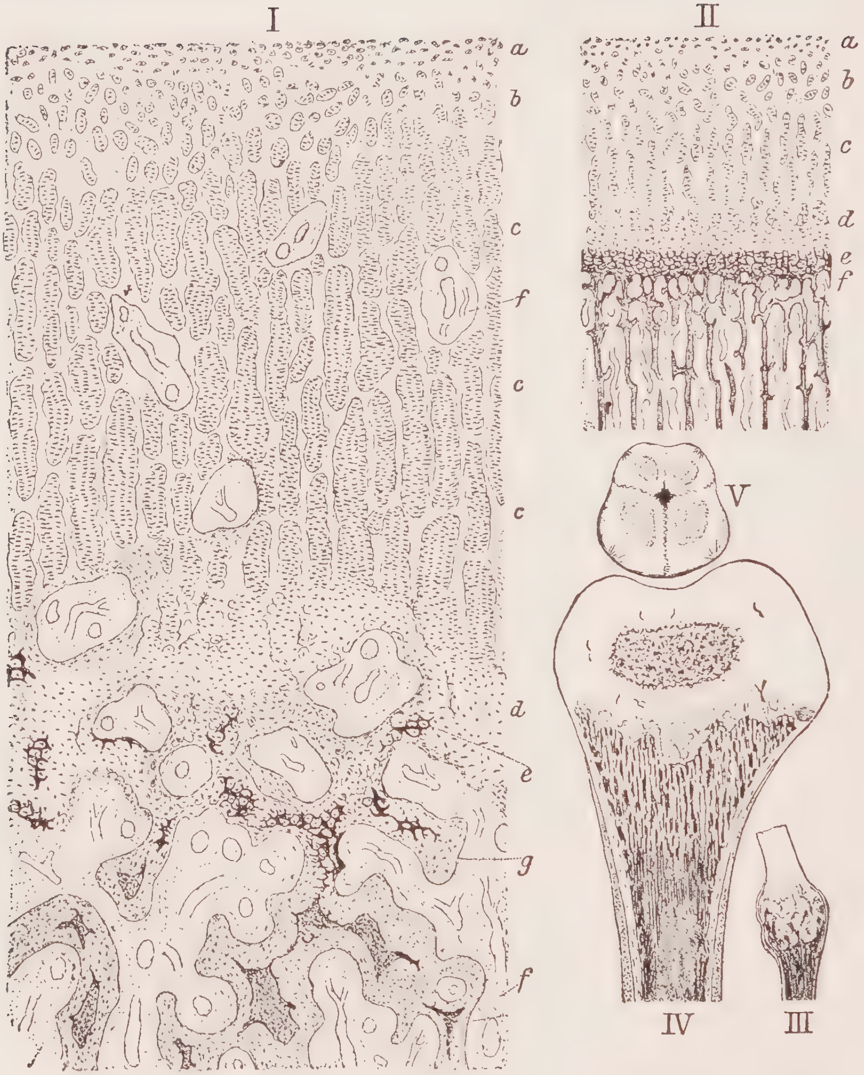
The disturbance of enchondral ossification is particularly striking and valuable in the macroscopic diagnosis of rickets, inasmuch as the layers grow into each other, but in the entire skeleton only in severe cases (Pommer). Those bones or parts of bones which grow the more rapidly (p. 1153), are first involved: ribs, lower part of the femur, upper end of the humerus. This disturbance of enchondral ossification is the chief differentiation of rickets from the clinically different, but morphologically similar, osteomalacia.

If a section of a rachitic bone at the epiphyseal border (fig. 588 and fig. IV, p. 1156), is compared with that of a normal bone (fig. C, p. 1134), it shows the following macroscopic differences:

(*a*) Swelling, transparency, blue red color, soft consistency of the cartilage, and enormous spread of this into the growth zone.

(*b*) The border of ossification is entirely irregular, and zigzag. The normal, yellow white, linear zone of calcification is lacking, and is represented only here and there in the blue red swollen ground substance by white spots of calcium.

(*c*) In the normal, the invading marrow vessels produce a straight red line; in rickets, red spots, papillae, and vessel trees coming from the



FIGS. 589–593.—I. Rickets. Longitudinal section through ossification border of upper end of diaphysis of femur; from a child 1 year old. a, cartilage normal, resting; b, moderately proliferating hyalin cartilage; c, long columns of proliferating regulated cartilage cells (cartilage cell pillars) this zone is shortened in the illustration; d, zone of large cell cartilage without pillar arrangement; e, calcified cartilage ground substance; f, vascular marrow spaces (mostly cartilage marrow canals) which progress far into the proliferating cartilage; g, osteoid tissue, formed partly directly from cartilage but mostly from the marrow. Here and there are remains of old bone trabeculae, in other places remains of calcified cartilage (black); in the center are osteoid tissue columns (med. magn.). II. Normal boundary of ossification of upper end of diaphysis of femur (normal enchondral ossification), child ½ year old. a, resting hyalin cartilage; b, zone of beginning cartilaginous proliferation; c, directed cartilage cell pillars; d, pillars of hypertrophic cartilage cells; e, zone of preparatory calcification; f, zone of first marrow spaces (see fig. VI, on p. 1060). Then follows the zone of bone formation. Low power (see text, p. 1151). III. Rickets: transition from cartilaginous to bony rib; nat. size. IV. Rickets: of moderate degree; lower end of femur; soft periosteal osteophyte, child 1½ years old; nat. size. V. Rickets: osteophyte on frontal and parietal bones of 4 years old child; fontanell still wide open.

hyperemic, dark red marrow in irregular branched figures, appear far in the soft cartilage. In addition, the so-called cartilaginous canals or cartilage marrow canals (p. 1135), produce vessels, which, according to M. B. Schmidt, are present from the very beginning; they find their way through the ossifying layers of the cartilage, and divide it into tongue-shaped territories. The cartilage which remains is changed into osteoid by metaplasia. This osteoid tissue will again be met under (*f*). According to Schmorl, this activity of the cartilage canals appears only in advanced and severe rickets; the cartilaginous canals lie one above the other like the stories in a building and this is more frequently observed in the rachitic cartilage zone, because the cartilage canals which in normal ossification enter the marrow as soon as they have reached the border of ossification, persist in this disease.

(*d*) Other marrow cavities invading far into the cartilage and surrounded by osteoid trabeculae, are recognized macroscopically as gray white stripes. They enter from the zone of osteoid tissue into the soft cartilage as mentioned under (*f*).

(*e*) Those trabeculae which lie around the irregular marrow cavities are soft, osteoid, and not bony as normal. The osteoid trabeculae may vary in thickness, according to which the marrow cavities are wide—the ordinary picture—or narrow. Here and there islands of unchanged cartilage remain between the marrow cavities and their osteoid tissue.

(*f*) Between the cartilage and the hard bone there is often a zone of finely porous osteoid of varying thickness, from a few millimeters (fig. IV, p. 1156) to a number of centimeters (fig. 588). This zone is elastic to a certain extent. The osteoid is nearly all chondroosteoid produced by metaplasia of the unused cartilage (see under *c*), and as an endosteal product. It helps in the swelling of the epiphyseal ends, and in the formation of the so-called "double joints" (fig. 588).

Thus the chief points of departure from normal endochondral ossification are:

1. Much diminished calcium deposit, and, as a result, defective or complete lack of a preparatory zone of calcification. 2. An increase in extent and softness of the zone of cartilage growth, with swelling at the border between the epiphysis and the diaphysis. 3. Irregular invasion of richly vascular marrow cavities and also cartilaginous canals deep into the cartilage. 4. The appearance of soft osteoid tissue in various amounts, which, on the one hand, produces a broad zone between the bone and the cartilage, and, on the other hand, stripes in the soft cartilage.

In detail, the microscopic examination of the pathological changes at the border between the diaphysis and epiphysis shows the following:

An important enlargement of the cartilage growth zone, particularly of the columns of cartilage (fig. 589, I). If we start from the resting cartilage, we see that the cells are growing mildly in the capsules (fig. 589, 1B), but increasingly into the diaphysis, so that there appear colonies of fifty or more cells one behind the other in a capsule, (fig. 589, 1C). Then the cells are separated, the division into columns disappears, and finally toward the diaphysis, there are isolated large, single cell cartilaginous capsules. These cells are very rich in glycogen (technique of demonstration on p. 950).

It is probable that there is no absolute increase due to overgrowth, particularly not in the so-called hypertrophic layer, (Pommer), but merely a relative broadening of the cartilage produced by the slow disappearance of the cartilage by invasion of the bone marrow and its change into bone (Schmorl and others), a view which Erdheim confirms. Thus the cartilage lies dormant and does not undergo its ordinary reconstruction (Looser, lit.).

Islands of calcification can be found only here and there in the cartilaginous ground substance. What is particularly striking, however, are the cartilaginous marrow canals, vessels and spaces (*f*), often macroscopically visible as they are shoved far into the uncalcified cartilage; these come from the richly vascular marrow, which, however, is poor in actual marrow cells in its subchondral layers, and which contains foci of osteoid tissue. The large cell cartilage is changed indirectly to cartilaginous bone, *i.e.*, into osteoid tissue.

Then beyond the cartilage is a layer of varying thickness (*d*), in which the osteoid tissue is entirely irregular and there is little resemblance to ordinary bone structure (zone of osteoid tissue).

In very severe cases (as in fig. 588), the spongioid-osteoid tissue is abundant enough to resemble a myelogenous callus.

Between the foci of osteoid tissue are large spaces filled with marrow rich in spindle cells. This marrow (endosteum) also produces osteoid tissue and further thickens the irregular trabeculae. But islands of unchanged cartilage can always be found here and there in the osteoid zones, even macroscopically (fig. 589, I).

Islands of cartilage are still retained when the rachitic process has disappeared, and they may finally give rise to multiple cartilage tumors (Virchow).

Internally the osteoid enters a zone in which calcium salts have been deposited in the centers of the osteoid trabeculae.

Microscopic Processes in Beginning Rickets, in Remissions, and During Healing.—Pommer recognized circumscribed defects in the preparatory zone of calcification as the first changes in endochondral ossification in macroscopically non-diagnosable, beginning rickets. Schmorl confirmed this discovery of focal calcium defects. (Such cases are determined to be rickets by the finding of osteoid seams, p. 1153.) These changes are first visible in the ribs, (p. 1155). If, on the other hand, there is a longer persistence or a broadening of the zone of calcification, it is an expression of remission and healing, the restituted calcification of the cartilage appearing not at the epiphyseal borders, but as a zone in the cartilage itself. And this zone of calcification is shoved toward the cartilage far up into the first vessel layer which persists in the cartilage (p. 1155, Schmorl). Non-calcium containing bone is no longer present, or present merely in traces, for during healing the non-calcified bone undergoes calcification, or is destroyed and replaced by new, rapidly calcifying osteoid (p. 1153), unless a beginning rickets, or a new exacerbation of the disturbance of the growth sets in soon after healing, again characterized by osteoid seams.

The reason for the nutritional disturbances in rickets is still undiscovered despite much investigation. It is, however, quite probable that rickets is at least favored by an insufficient dietary composed chiefly of carbohydrates. An intestinal catarrh often precedes rickets. Anemia precedes and accompanies the process. There is a leucocytosis; other blood changes have been described. A chronic splenic tumor is frequent; according to Beneke, the liver also is frequently enlarged. The right ventricle is often hypertrophic without apparent cause.

Many hypotheses have been offered to explain the details. The diminished calcium deposit has been thought due to insufficient intake (Zweifel), or insufficient absorption following gastro-intestinal catarrhs, etc.; the decalcification of the bones has been thought due to an overproduction of lactic acid in the blood, a factor which, as the assumption of increased acid formation in general, must be disregarded in the development of rickets (see the interesting experiments of Schloss, lit.). The decalcification hypothesis is contradicted, because halisteresis is not typical of rickets, nor does it play a large part in the disease, and also because the amount of acid produced is not sufficient. Among other things, it has been thought that lactic acid hinders the absorption of calcium salts. Rudel (see also Vierordt) showed, however, that as far as the excretion of calcium is a measure of its absorption, there is no change in rachitic children. Also, according to Pfaundler, the calcium intake, absorption, metabolism, and the alkali of the blood, are not particularly changed; he speculates that the "calcium fixers" (bone and cartilage cells), function insufficiently; too little calcium salts are deposited in them, or insufficiently fixed, because, for some unknown reason, they lack the specific affinity for calcium salts (see also Nathan). Dibbelt, on the other hand, believes that the pathogenesis is a disturbance of the calcium metabolism in the form of an increased excretion of the metal through the intestines without it producing general digestive disturbances.

Animals fed on diets poor in calcium show no changes similar to those of rickets, but rather an osteoporosis (see among others, Gotting, Oehme, lit.). This is also true of Dibbelt's experiments. On the other hand, according to Oehme, a process more similar to rickets is produced when strontium phosphate is given to a growing dog fed on a calcium-poor diet, the explanation of which is said to be a slowness of absorption and the acquisition of a vigorously increasing activity by the strontium. According to Lehnerdt, newly formed osteoid tissue undergoes calcification if sufficient calcium is given even when fed with phosphorus or strontium, so that the net result is sclerotic bony tissue.

Kassowitz believed that the hyperemia of the bone marrow indicated an inflammatory process at the bottom of rickets, and this hypothesis tries to explain both the increased cartilaginous and bone growth and the increased resorption. It also is said that the increased amount of blood gives the salts no chance to precipitate, or if they were "fixed," they are readily washed away. Many think of an infection (Hagenbach, and the animal experiments of Mircoli and particularly Morpurgo, see p. 1081). In young dogs, J. Koch (lit.) produced hematogenous inflammatory foci in the growth centers of the bones by injecting streptococci, following which there were rachitic changes; he thus believes that an infection is the cause of the spontaneous rickets of dogs, but he also attempts to extend these experiences to hunger malacia, called by others, late rickets, and other such bone softenings (p. 1072). The infectious theory seems not improbable to Looser; he points out, among other things, the fact that, of a number of brothers and sisters living in the same poor dietary circumstances, only one acquires late rickets; and Schloss (lit.) believes that Koch's experiments explain at least certain cases in which the outbreak of the disease or an exacerbation was obviously subsequent to an infectious process, whereas in the majority of cases of rickets, the etiology is in the direction of a general disturbance of metabolism and nutrition. (For the infectious theory, see also Selter.) Kubo and others, on the other hand, believe it has not been demonstrated that human rickets was ever produced by such processes, particularly not by the activity of bacteria. Others speak of an intoxication. Stoeltzner's hypothesis relates rickets and osteomalacia to a functional insufficiency of the adrenals (see opposed Schmorl, who found no changes in the chromaffin system), and he points to Bossi's good results in the treatment of osteomalacia with adrenalin (results not constant, see Looser). But the relationship of the glands of internal secretion to rickets has not been solved.

The rachitic changes in animals (young rats), following thymus extirpation have been mentioned on p. 497; those following extirpation of the parathyroids, and the debatable meaning of the increase in size of the parathyroids in the spontaneous rickets of rats (Erdheim), were discussed under the parathyroids, p. 540. According to Erdheim, rickets and osteomalacia are caused by a pathological diminution in size of the parathyroids (Weichselbaum). The alleged etiological relationship of rickets to lues is discussed by Caffarena. v. Hansemann emphasizes the influence of domestication, *i.e.*, culture (living quarters, clothing, nutrition), since rickets is said not to occur in uncivilized peoples. According to Wieland, the most important factor is heredity. Siegert and Schloss (lit.) also believe that there is a familial factor to be considered.

Lit. concerning rickets in appendix.

When rickets heals (usually with remissions, and after a duration of one or a number of years), the osteoid tissue gradually undergoes calcification beginning in the centers of the trabeculae. But in time this bone disappears and is replaced by good osteoblastic bone coming from the marrow, so that finally the latter cannot be differentiated from that produced normally. The endochondral ossification returns to normal, and, as stated on p. 1159, the preparatory zone of calcification reappears. Mild degrees are healed without trace, but in severe rickets, the bones are bowed, lumpy, heavy, and ivory-hard. The marrow spaces may disappear almost completely (rachitic eburnation). Ossification of the osteophytic deposits leads to thickening of the flat bones. When the growth of a bone remains stationary after disappearance of the rickets (occurs particularly in severe cases), it (especially the thigh), remains permanently small. The result is an underdevelopment and a dwarfism, (rachitic dwarfs).

Consequences of Rickets.—The rachitic bone is poor in calcium and earthy salts, rich in water; its specific gravity is diminished. When the changes are marked, the entire bone becomes soft and flexible like rubber. The hypertrophic cartilage and the osteoid are always flexible; when the calcium deposit is incomplete and the cortex is thin there is a tendency to infractions, or to kinkings occurring usually on one, *i.e.*, the concave, side, so that the wall angulates into the marrow cavity, like the kinking of a quill (Virchow). The weight of the body and muscle pull are the most important factors in producing these deformities.

Changes in Individual Parts of the Skeleton.—(Many details of this condition are taken from the comprehensive work of v. Recklinghausen published posthumous.)

The long tubular bones in florid rachitis show grave swellings at the diaphyseal borders, producing the so-called double joints. As a result of the softness of the cartilage and the osteoid tissue, the epiphyseal ends are displaced and bend away from the shaft. Tears and relaxations of the ligaments of the joints are common (genu valgum); the shaft may be bent like a bow; in the thigh, for instance, the convexity is directed internally (fig. 594); in the bones of the lower legs, the convexity is usually directed externally (saber leg), or frequently anteriorly. As stated, the weight of the body and the pull of the muscles are important in producing these deformities. The shaft may be kinked (infraction), or actually fractured; very marked bowing, most frequently of the femur, is probably caused by infractions. These infractions and fractures occurring not only in the long bones of the lower extremities, but also in the ribs, heal slowly by the formation of callus which may remain partly cartilaginous. The entire angle of the kink is filled with the callus; static causes produce the thickness of the cortical layers on the curved side; the marrow cavity

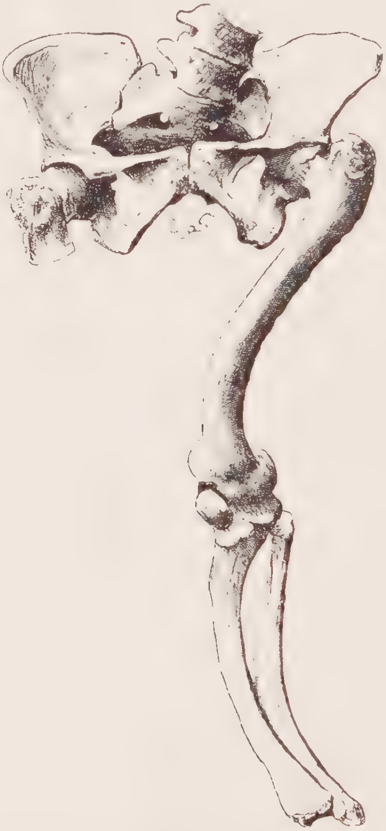


Fig. 594.—General and oblique narrowing of pelvis due to severe rickets; marked left-convex scoliosis and lordosis of thoracic and lumbar spinal column. Marked lateral and axial curvature of upper and lower leg. 74 year old woman. Obvious arthritis deformans.

itself is occasionally filled, and later becomes hollow again. In healed rickets, the bones, especially the tibiae and the fibulae, often show flattening of their diaphyses (fig. 594); they become like sabre sheaths (tibia en lame de sabre), sharply angulated and very hard (osteosclerosis); the double joints disappear; milder degrees of bowing are straightened by functional rearrangement of the bone. The growth in length of the lower extremities is often inhibited, while the trunk reaches its normal size (rachitic dwarfism). If the intermediary cartilage is examined after rickets has ceased, an irregular angular course of the line of ossification may be followed for many years, *e.g.*, for nineteen years in a preparation in Breslau.

The bony and cartilaginous unions of the ribs become nodular and thickened along the sternum (rachitic rosary). Merely a wall-like protuberance is physiological. From bending and displacement of the cartilage, the thickening is sometimes directed internally into the thorax (internal rosary). Through the sinking in of the ribs internally, the breasts become smaller, the breast bone becomes wedge-shaped or like the keel of a ship, as the so-called pectus carinatum or gallinaceum—pigeon breast—produced by the pressure of air and the inspiratory diaphragmatic pull on the ribs. Occasionally there is an anterior, bowl-shaped, sometimes bilateral, sinking in of the thorax from multiple infractions of ribs.

The relationship of the so-called funnel breast to rickets is no longer recognized. The funnel breast consists of marked depression of the lowest part of the sternum with a funnel-shaped pulling in of the anterior wall of the breast, which in stout women is a furrow. This condition is a congenital growth anomaly, to which an occupational factor may be added (shoemaker, tinsmith, tailor, etc.). (Lit. by E. Ebstein and Verse.)

Rachitic scolioses, kyphoses, and lordoses (bowing laterally, posteriorly and anteriorly), occur in the vertebral column from body weight and muscle pull; these produce important asymmetries of the thorax (p. 1265). Probably most scolioses are produced by rickets. A mild bending of the thoracic part of the vertebral column to the right is called a physiologic scoliosis. The rachitic kyphoses and scolioses are usually obvious exaggerations, or caricatures, of the physiologic bowing (p. 1265). Pott's spine, caused by caries, can be differentiated from rachitic kyphosis, among other things, by the fact that it usually occurs with a shortening of the legs.

Deformities of the pelvis are of great practical importance. If the synchondroses of the sacrum, the iliae and the symphysis are too movable, the pressure of the trunk is directed toward the promontory. The true conjugate (the line between the promontory of the sacrum and the symphysis) is short. In the normal adult female pelvis it measures eleven centimeters; in such cases it may be diminished to four centimeters. The pelvic entrance becomes kidney-shaped. This is the flat rachitic pelvis (fig. 594). The arch of the pubis is very wide, the tuberosities of the ischii are pushed apart, the acetabuli point more forward. The ventral surface of the ilium is small and flat. If the other synchondroses, namely, the three-rayed cartilaginous unions between the os pubis, the ischii and the ilei are abnormally movable, and if the other part of the pelvis is soft and elastic (as in severe cases), the pressure of the trunk, and the counter pressure of the heads of the femurs, produce a transverse narrowing; thus the pelvis is generally narrow or asymmetrical, the aperture of the pelvis becomes three cornered or clover leaf shaped, the pelvis resembles that of osteomalacia (p. 1078), and shows a snout-like protuberance of the pubis. This pseudo-osteomalacic pelvis is not always easy to differentiate from a true osteomalacic, formerly normal, pelvis. According to the severity of the case, the pelvis remains small and tender, or becomes very plump and heavy. There are many sharp pointed prolongations and exostoses, particularly where the muscles are inserted, but also in the neighborhood of the joints. For details see the classical work of Breus and Kolisko.

The skull, even though not always, is often involved in a decided manner.

The fontanelles remain wide open and the sutures are broad because of the irregularity in bone growth, most marked when there is coincident hydrocephalus (hydrocephalus rachiticus). The large fontanelles close normally at twenty months; they remain open from three to four years (fig. V, p. 1156). See p. 1154 for the severe malacic forms.

The most frequent change in the bones of the skull is periosteal osteophytosis on the external surface. The internal surface is glassy and hard, shows deep impressions and high juga cerebralia. Very delicate or pumice-like, richly vascular, osteoid deposits, occasionally arranged in parallel lamellated lines, remain uncalcified for long times, but later, when the process undergoes regression, become bone and produce thick deposits externally to the extent of many millimeters. These periosteal overgrowths do not spring from the suture or the points of ossification, but ordinarily appear in the edges of the bones, so that the sutures and the tuberosities remain free (fig. V, p. 1156); a symmetrical arrangement is characteristic (v. Hansemann).

When the completed hard bones of the skull are involved, they are thinned by resorption from the inside outward by the pressure of the growing and venous hyperemic brain, whereas, on the outside, merely soft osteoid tissue is deposited instead of normal firm bone; thus there are thin places which still contain old, more or less compact, bone, but perhaps kinked, infracted, and compressible like parchment; in other cases, resorption of the old bone proceeds still further, and becomes total, so that soft osteoid places appear in the roof of the skull. Formed membranous spaces may also appear, inasmuch as a considerable number of layers of the soft osteoid tissue disappears from the pressure. Occasionally the roof of the skull becomes like a sieve corresponding to the prominences of the convolutions. Even membranous spaces are developed, particularly often in the posterior skull (the so-called soft posterior head, cranio-tabes, Elsasser, with supraoccipital zones of softening), caused not only by the pressure of the growing brain, but also by the counterpressure exerted by the pillow, etc., on which the head rests. This is called cranio-tabes rachitica. But Wieland disputes the relationship of the congenital soft, or perforated skull to rickets, and believes it is due purely to mechanical pressure by the rapidly growing brain toward the end of the fetal time; he demonstrated a lawful regression and an increasing hardening, which can be subject to secondary involvement only, of an ordinary, always post natal, rickets (cranio-tabes). v. Recklinghausen also believes that the hypoplastic bones of the skull in newborns and sucklings may be caused without rickets; but he does believe that the typical soft posterior head is a sign of rickets, an idea which Kassowitz confirms, and which Schloss also recognizes. Thus, there occur simple hypoplastic or atrophic conditions which Thoma calls hypostosia, observed as congenital spaces, vesicles and the relief skull, not rarely combined with rachischisis (spina bifida, see fig. 595), which should be differentiated from cranio-tabes rachitica. In rachischisis, M. B. Schmidt occasionally found a pathological bas-relief of the convolutions apparent upon the non-hydrocephalic skull. The more marked the hydrocephalus, the more marked the osteophytic overgrowths, so that after rickets has run its course, and when the osteophytes are changed into sclerotic bone, the children's heads are very large and thick. Thus rickets often leaves permanent changes in form; the skull is large in relation to the face; the shape may be four cornered (tete carree). The sclerosed four points of ossification in the frontal and temporal bones retain their bowing, and on further flat growth of the skull, which occurs along the sutures, are pushed upward as four fixed corners, while the parts remain flat between the four points. The base of the skull is also hindered in its growth and shortened, particularly in hydrocephalus. Therefore the base of the nose is very deep. The bones of the face may be likewise involved. The upper jaw may be angularly kinked at its insertion into the zygomatic arch. The rims of the alveoli are soft, the first teeth appear late and soon fall out, the permanent teeth are crooked (irregular dentition) and soft. Concerning the relationship of enamel hypoplasia to rickets, see p. 584.

So-called rachitis tarda is actually rickets in some cases, (Mikulicz; Schmorl found osteoid seams and typical cartilage lesions), osteomalacia in others (or alleged ostitis fibrosa), which appears for the first time, or is a recurrence of rickets after the fifth year, occasionally even at the time of puberty; during the physiologic rearrangement of bone, new bone remains uncalcified for long times (for osteofibrosis, see v. Brunn). The condition occurs chiefly in anemic individuals and often leads to deformities (scoliosis, genu valgum, coxa vera, see under those diseases). According to Looser, (lit.) juvenile osteomalacia is identical with late rickets, and is characterized by absence of calcium in new bone, by atrophy of bones, and rachitic disturbances in the cartilage. See collected references by Wieland, Christeller, Bittorf, Szenes. See also the lit. under hunger malacia of the bones (p. 1072), which, according to Fromme, is a form of late rickets. [For the parathyroids and rickets see Hammett F. S. Endocinology 8: 557: 1924.—*Translator.*]

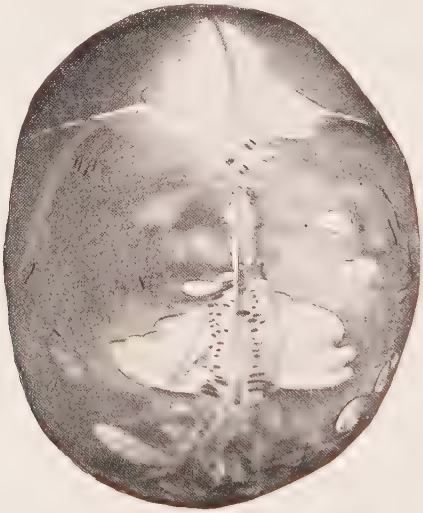


FIG. 595.—Non-rachitic open skull of a newborn with internal hydrocephalus and spina bifida. Numerous openings, especially large on parietal eminence; wide sutures, wide, large fontanell; about ¾ nat. size.

For changes in the musculature in rickets, see Gutstein, lit. [For further data and lit., see Howland J. Medicine 2: 34: 1923 and Ergebn. d. Physiol., 25: 517: 1926.—*Translator.*]

Moller-Barlow's Disease (Scurvy of Childhood).—For scurvy of adults, see Aschoff and Koch. This disease was first described by Moller in 1859, and believed to be acute rickets; it has recently received much study; it occurs chiefly in artificially fed sucklings, *i.e.*, those fed with overheated milk and substitutes, during the second half of the first year of life, but may appear up to the eighth year (Eug. Fraenkel); in older children there seems to be a certain predisposition toward the disease, a statement which holds good for the scurvy of adults. The symptoms are striking pallor, bloody suffusions around the gums, severe pains, and swellings (subperiosteal hemorrhages) in the ribs, which may lose their tight union with the sternum (Eug. Fraenkel), in the lower extremities, particularly the thigh and the shin bone, rarely the tibia or fibula, hardly ever of the upper extremities, and rarely in the skull (but most frequently there in the roof of the orbit; Eug. Fraenkel). The bones are hindered in their growth, become porous, and tend to show fissures, infractions, or even fractures, as well as displacements, particularly at the ends of the diaphyses, with impactions of the cartilage into the brittle diaphyses (Hart). The chief signs are the hemorrhages, particularly into the marrow and periosteum which may be lifted off almost as though by a tumor; particularly large hematomas are due to separation of the continuity of the epiphyseal borders from the shafts (fig. 596). Hemorrhages also occur in the skin, the mucous membranes, the mouth, the conjunctivae, the intestines, the pelvis of the ureters, the bladder (bloody urine! see Heubner, lit.), more rarely the cheeks (Weiss, lit.). The changes described in the skeleton are exceedingly diverse, with more or less analogy to rickets, syphilis, osteogenesis imperfecta, etc.; others believe the disease is entirely independent of rickets (Nauwerck, Schmorl and others), but recognize that both diseases may be present in the same patient at the same time. Thus there is a reason why the anatomic findings vary in detail in this clinically well defined disease of childhood, and why there has been a number of interpretations. A change common to all cases is a pathological condition of the bone marrow, particularly around the cartilaginous borders, where it becomes a poorly cellular mass, meshy, finely fibrous and poorly vascular, (Naegeli, Schodel-Nauwerck, Schmorl, and others); this sign makes obvious (Orth, Eug. Fraenkel) the primary and most important of changes in pure cases, and in those artificially produced in animals by insufficient dietary. Herzog believes that circulatory factors in the cartilaginous border are the initial causes, disturbing the lawful development and function of the bone forming elements, the cause of both being noxae, arising as a result of insufficient nutrition. Ziegler, who calls the process "osteotabes infantum," believes the changes begin with rearrangement of the lymphoid (splenoid) marrow in the so-called skeletal marrow (Schodel-Nauwerck). Accompanying this inability to build bone and disturbed enchondral ossification because of insufficient vascularization (Schmorl), there is also vigorous resorption, even though it probably does not overstep the physiological limits; thus there remain calcium trabeculae and calcium spicules to abnormal extent, because the ability of the bone marrow to destroy the excess is less than normal in the zone of calcification (Nauwerck). In these calcified lines of cartilage, insufficient bone is deposited. The cortex becomes thinner and thinner since apposition disappears, and resorption continues. Thus is explained the fragility of the tubular bones, their collapse, their solutions of continuity (fig. 596), particularly along the epiphyseal-diaphyseal borders, the "ruins" of Eug. Fraenkel, and the breaking off of the cartilaginous from the bony parts of the ribs. Hemorrhages then occur into the marrow and periosteum, which, as stated, lift off the latter, and surround the bones like a cloak (fig. 596). When the disease has lasted for some time, periosteal bone deposit does occur.

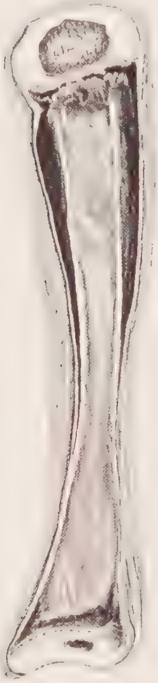


FIG. 596.—Moller-Barlow disease. Frontal section through tibia; a bone nucleus in each upper and lower epiphysis; in the proximal shaft bordering the epiphysis in zone of necrotic destruction a break in continuity, the cleft filled with blood. The periosteum is lifted off down to below the middle of the diaphysis by a hemorrhage enveloping the bone; less change at distal end; ¾ nat. size.

The nature of this disease is now better recognized. It has nothing in common with rickets (that is, as a hemorrhagic form), nor with an infection, if only because there are no osteoid seams in the pure cases of scurvy (Hoffmann, lit.; concerning various findings which may resemble rickets, see Hart). Nevertheless, the combination of rickets with scurvy is quite frequent, (in about half of the cases; Schmorl, Eug. Fraenkel; v. Recklinghausen), as shown by newer investigations with especial emphasis on this relationship. Looser (lit.) calls the disease "suckling scorbutus" (see Neumann); Eug. Fraenkel (lit.) enlarges the definition and speaks of "infantile scorbutus."

Experimentally, Holst and Frohlich fed guinea pigs a qualitatively insufficient dietary of bread and certain grains, and produced a picture similar to human scurvy, including the characteristic bone changes (see Ingier). Lipschutz and W. Huebner saw similar bone changes in dogs fed on diets poor in phosphorus (O. Heubner), but Schmorl does not believe the condition is completely identical to Moller-Barlow's disease. The experiments of Hart in which he fed condensed milk to monkeys must, however, be considered evidence that it is possible to experimentally produce the classical symptoms of scurvy.

Looser reached the opinion that the cause of the disease is a hemorrhagic diathesis following chronic disturbance of nutrition; he believes specifically that the fibrous bone marrow is a consequence of the hemorrhages, as the atrophy of the spongiosa, and the corticalis are consequences of the subperiosteal and marrow hemorrhages. But Eug. Fraenkel and Schmorl do not accept the hypothesis of Looser (Barlow), *i.e.*, of the secondary nature of the fibrous marrow, but rather believe that the hemorrhages are a symptom independent of the characteristic changes of the bone marrow, and merely a part of the hemorrhagic diathesis. v. Recklinghausen called attention to certain peculiarities of the blood vessels of the marrow (luxuriant bulbous growth of the capillary vessels), which probably help cause the hemorrhages. The administration of a correct diet cures the great majority of cases in a few months. Dead material is removed from the "area of ruin" by giant cells, the marrow again becomes lymphoid, and new bone substance is constructed (Eug. Fraenkel, Ingier). But deformities may result such as varus- and valgus positions of the upper in relation to the lower leg, or even coxa vara.

Concerning Barlow hearts, and the hypertrophy of the right ventricle resulting from interference with respiration caused by lesions in the ribs which do not allow proper emptying of the right ventricle, see Erdheim.

Defects, Hypoplasia and Hypertrophy of the Skeleton.—Defects of the bones are related to the circumstances that parts are not laid down in the very beginning (aplasia), or development is hindered during intrauterine times, or parts already existing are made to disappear. (Extensive lit. by W. Kummel.) Entire bones, parts of the roof of the skull, parts of the vertebral arches, entire bones of an extremity, such as the fibula, radius, humerus, femur, may be absent, producing short members, micromelia, (fig. 597); or merely parts of these bones are defective, especially the ends of the radius, ulna, tibia, etc. In hypodactylia, one finger is lacking, often an hereditary malformation (Schroeder, lit.). A typical malformation from defect is phocomelia, wherein the middle parts are entirely or partly absent; the hands and feet are normal in size, but are inserted more or less directly into the shoulders or the pelvis. According to J. C. Saint-Hilaire, the hands and feet inserted directly into the trunk are merely rudiments in hemimelia; in ectromelia (amelia) there is not even a trace or rudiment, (lit. by Apert, Socin).

Insufficient Growth in Length of the Skeleton.—Inhibition in the growth of the bones (hypoplasia of the skeleton) occurs (*a*) in intrauterine life, or (*b*) is noticeable in the growth after birth.

In those present at birth, *i.e.*, hypoplasias of the skeleton developed in the uterus, the shortness is chiefly of the extremities (micromelia), while the soft parts are normally developed, and therefore relatively too broad and too long for the extremities. The skin is folded like a dress with too much cloth; it is edematous or merely very fatty, and Beneke believes it exerts a growth inhibiting pressure upon the skeletogenic tissues. (See also Wiesermann, and the negation of this view by Sumita and by Murk Jansen.) The great majority of these cases were erroneously called fetal rickets, or perhaps micromelia chondromalacia. The name introduced by the author fits the condition better—chondrodystrophia fetalis, (fig. 598), since the changes depend on incomplete growth of the cartilage and early cessation of enchondral ossification. The older designation, achondroplasia, Parrot, 1878, is still used almost exclusively in France, Porak-Durante and the references of Schirmer and Wieland, lit. But this term is not used by the author since it gives the false impression that no cartilage at all is formed, and is entirely absent; for instance, the term thyreoaplasia is used when the thyroid is entirely absent. For those who still hesitate over the term chondrodystrophia, it might be mentioned that Parrot, who first showed the error of "fetal rickets," and proposed the term achondroplasia, and also Pierre Marie (la Presse Medical, 1900),

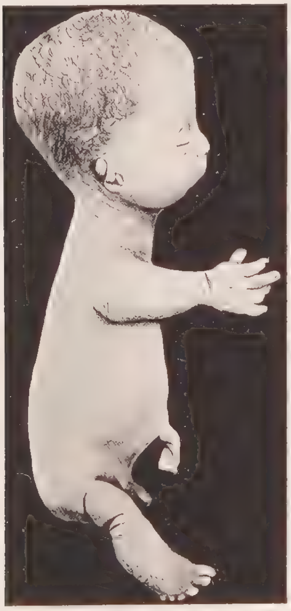


FIG. 597.

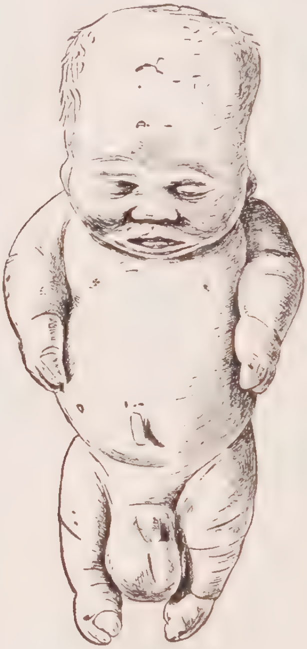


FIG. 598.

FIG. 597.—Micromelus, 6 months fetus with numerous malformations. Micrognathia, malformation of ear; hexadactylia (6 toes); total defect of femur and fibula; tibia rudimentary; humerus absent; both fore arm bones articulate with shoulder joint; absence of corpus callosum. (Details in I. Diss; B. Schwendener, Basel, 1899.)

FIG. 598.—Fetal chondrodystrophy (malacic form) causing micromelia; head thick, nose, as a whole, flattened; no special contraction of nasal root; no synostosis of tribasilar bone; the sphenobasilar synchondrosis broad and soft; right inguinal hernia. (This case and three others described by B. Schwenderer. Unters. ub. d. Chondrodyst. foet. I. Diss. Basel, 1899.)

express themselves in this way: "que l'achondroplasie est caracterisee par une dystrophie decartilage primordial." Poncet and Leriche also agree that the term chondrodystrophia describes the changes better than achondroplasia, (see also Fuchs, concerning the nomenclature). The diaphyses remain short, but because of relatively marked periosteal bone formation are more or less sclerotic. Kundrat therefore speaks of osteosclerosis congenita; but the sclerosis is not constantly present. The author differentiates three forms of chondrodystrophia, according to whether the cartilage, unable to produce sufficient longitudinal rows, is otherwise normal (chondrodystrophia hypoplastica), or is softened (chondrodystrophia malacia), or, rarest, is of normal hardness, but grows undisciplined and unprepared for the invasion of the marrow, and so that thick, broad, fungus-shaped epiphyses are formed on the short diaphyses (chondrodystrophia hyperplastica). According to Siegert, this last form may be shown roentgenologically to be combined with the hypoplastic forms. The hypoplastic form is the most frequent, and the author has shown degrees from mild to very severe, various amounts of shortening of the bones of the arm and legs (confirmed by others, Dufour; also clinically, J. Bauer). A vascular connective tissue strip coming from the periosteum is shoved in between the junction of the epiphysis and diaphysis. These periosteal strips have been subject to different interpretations (see the author, Sumita, M. B. Schmidt, v. Recklinghausen and others), but it is agreed that they interfere with growth in length; if situated on only one side of an epiphysis, *e.g.*, externally, the bone grows on the internal side, and thus becomes crooked. Dietrich believes they are a peculiar formation of the cartilaginous marrow canals (p. 1135), and are important both in the interruption of enchondral growth as well as in periosteal bone formation; they take over the function of growth in length, even though incompletely. Fig. 599 shows the condition at the epiphyseal-diaphyseal junction; the smallness of the zone of growing cartilage can be recognized, the formation of rows of cells is very weak, and the calcification zone broken through by marrow spaces is also small. The bone trabeculae are oriented very irregularly, and their growth is more in thickness and width than in length; the inclusions of calcified cartilage in the bony trabeculae are very small. The base of the skull is short because of cessation of growth of cartilage in the cartilaginous joints (sphenobasilar and intersphenoidal margins), or from simultaneous premature synostosis of these margins. The intersphenoidal margin begins to ossify at the time of birth, the sphenobasilar in the twelfth to the thirteenth year. This changes the profile of the face, and in the cases with synostoses (usually the hypoplastic form), the root of the nose is pulled in, and the face takes on a so-called "cretin-like" appearance; in the severe cases (malacic), in which the synostoses are lacking, the nasal region as a whole does not jut forward, but remains flat, (flat nosed individuals). Synostosis of the tribasilar bone is not necessarily present when there is "cretin-like" appearance of the profile; the latter may occur when the naso-maxillary parts that lie in front of the tribasilar bone are shortened. If these parts, on the other hand, are particularly well developed, there may be no pulling in of the root of the nose, in spite of premature high degree synostosis of the os tribasilare. According to Murk Jansen, an external pressure directed from before backward produces shortening of the base of the skull; in the flat nosed type, the direct pressure influences the entire face. The head is relatively large; the cerebral skull preformed, not in cartilage, but connective tissue, does not take part in the pathological process, but dilates as a compensation for the shortened base of the skull. The clavicles also take no part.

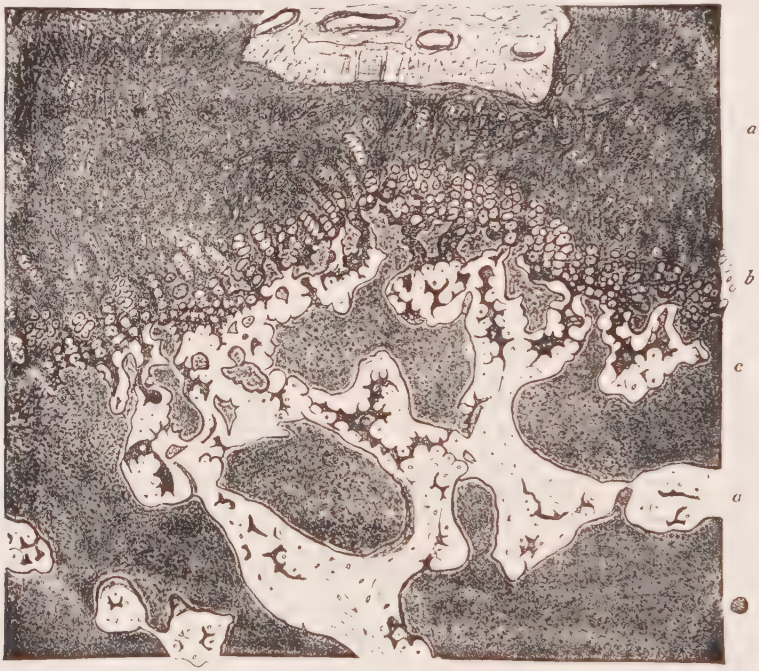


Fig. 599—Hypoplastic fetal chondrodystrophy; upper epidiaphyseal border of femur; a, cartilage; b, zone of proliferation and calcification; c, marrow; d, bone trabeculae with pronged inclusions of calcified cartilage (low power). (Dieterle, V. A. 184, 1906.)

These cases of chondrodystrophy which occur everywhere have been mistaken for cretinism (Virchow), and also for myxedema (for example, Moro). But there are fundamental differences (p. 1183). The etiology of the disease is unknown; perhaps it is caused by internal factors producing malformations, *i.e.*, a qualitative anomaly of the cartilage or germinal anlage of the cartilage, or perhaps it is an inhibition following ectogenic (amniotic) influences on the developing fetus. A causative role has not been demonstrated in the endocrine glands; in fact, they probably have no influence, because a unilateral chondrodystrophia is not at all rare. The disease is an hereditary, not rarely, familial disease (Chiari and lit. in appendix to p. 1175), which indicates an internal cause. Mechanical factors are blamed by Rindfleisch and v. Franque. Recently, Murk Jansen (lit.) has emphasized the same factors; he believes that the amnion is too narrow, and thinks he demonstrated a familial alternation of chondrodystrophia and other recognized amniogenic malformations; (see Duken). It is worth remembering in this respect, that the endochondral ossification was not disturbed in the micromelus, illust. fig. 597 (see Schwendener). In young rabbits, thyroid extirpation (p. 528), is said to

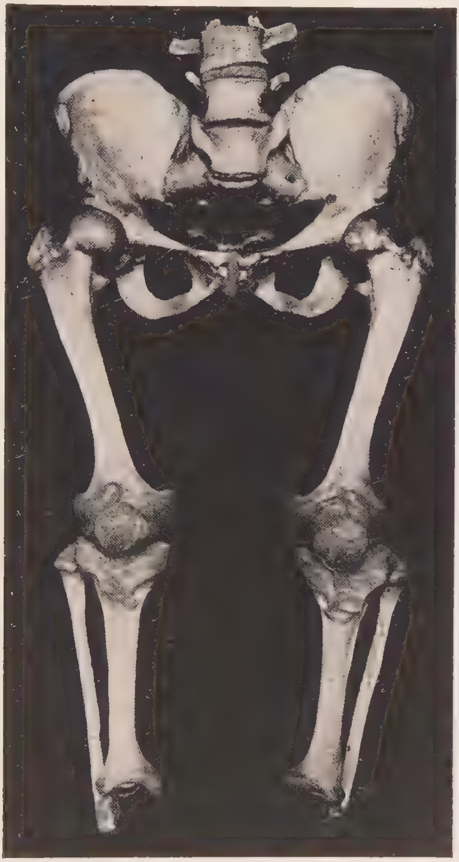


FIG. 600.—Chondrodystrophy (hypoplastic form); narrow pelvis. Upper and lower thighs of a dwarf who died after delivery by Cesarian section; 39 years old; body length 116 cm.

have caused cessation of growth and microscopic changes in the bones, which, according to Hofmeister, are similar to those of chondrodystrophy. The author and his pupils, however, showed that there were no changes in the thyroid gland in cases of chondrodystrophy, which negates the conclusion that removal of the function of this organ is an etiological factor (Schwendener); this statement has been confirmed by Sumita (lit.), who found no changes in the thyroids of chondrodystrophiacs; on the other hand, in a case of thyreoaplasia in a five months old child, we found changes in the skeleton which were not at all like those of chondrodystrophy, but had certain points in common with cretinism (Dieterle). Symmers and Wallace described cases of congenital chondrodystrophy (children of two, five, fifteen, twenty-five months, old), in which changes were found that they decided were "cretinish," and which they believed were due to changes in the thyroid gland, but there is no description of microscopic findings in the bones. A few cases have been reported in which humans with chondrodystrophy, all of them having a striking "family resemblance" among themselves, have lived for thirty and more, even eighty years (Porter; for tables and lit. see Siegert); but they usually die in the first few weeks of life. Those who live are usually healthy, plump, their members short, their legs particularly so, *i.e.*, they are disproportionate dwarfs (no taller than 140 cm., exception, the case of Porak, 150 cm.), with more or less bowed bones (illustrations by Breus and Kolisko, P. Marie, Weygandt), three-pronged hands, good, even exceptional muscular power, a somewhat "cretinic" expression of their face, which, however, is often lacking, a disproportionately large head, but without changes in their psyche; indeed, some of them have particularly high intelligence. In many cases, puberty is established very early with a hypergenitalism, and increased sexual power; this is supposed to be due to a disturbance of the hypophysis cerebri (Murk Jansen), but according to Duken, no changes in the internal secretory glands have been demonstrated. The hypophysis is frequently small corresponding to a small sella turcica; as examples, see the illustrations in the monograph of the author. The small space in the sella is a result of the shortening of the base of the skull, which, according to the author's opinion, is due to the primary dystrophy of the cartilaginous parts. Murk Jansen (lit.), on the other hand, believes an abnormal pressure is exerted by the amnion, which mechanically disturbs the shape of the skull. The well marked panniculus adiposis in many cases of chondrodystrophy, is believed to be an expression of an hypophyseal influence, an hypophyseal adiposity, but exact knowledge of these relations is lacking. If, however, the hypophysis is actually diseased, it does not necessarily follow that it is the cause of the dwarfism. Unilateral chondrodystrophic dwarfism (Siegert-

Nathanson) cannot be correlated with internal secretory influences whether thyrogenous, or hyperthyroidism of the mother (Abels), or genitalism following increase in function of the genital organs (Bertoletti), etc.

The chondrodystrophic dwarf pelvis was first described by Breus and Kolisko; it consists of marked flattening of the kidney-shaped pelvic entrance, markedly protuberant high promontory, almost horizontal tendency of the surfaces of the ileum, with plump edges, and early synostosis; the cretin pelvis, on the other hand, shows persistent joint margins. (Review by Hegar.) In the collection at Basel, the author found a pelvis coming from a dwarf who had died during childbirth by Caesarian section (clinical report by Reinhardt); this pelvis showed all the criteria of chondrodystrophy (fig. 600). (See also Falk, Engelmann.) Lordosis and lumbar kyphosis are sometimes coincident. Lit. in appendix.

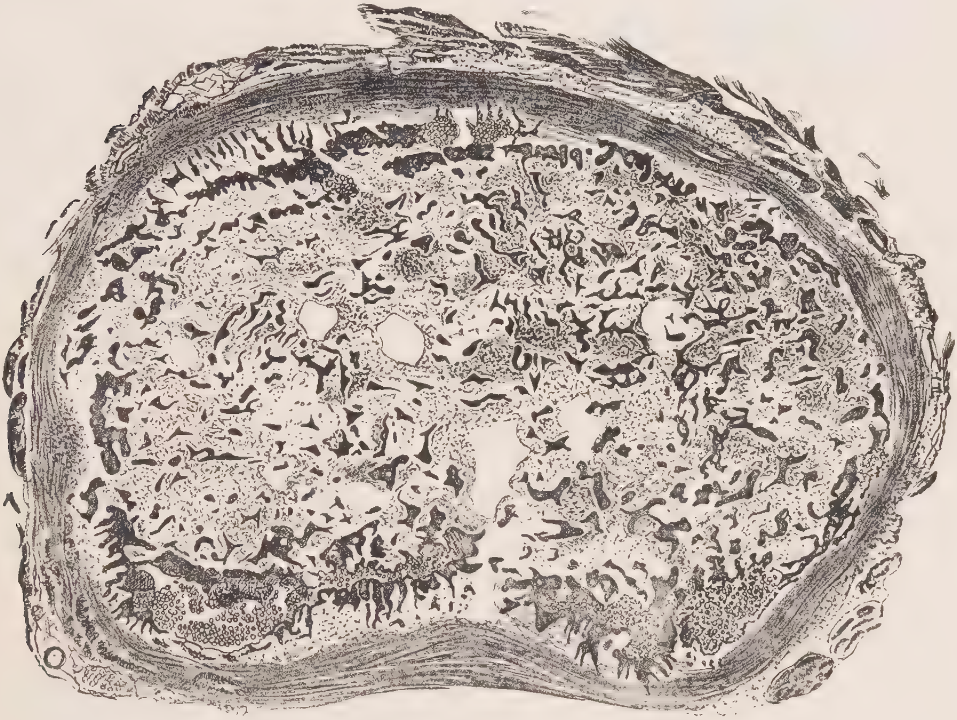


FIG. 601.—Imperfect osteogenesis; cross section through center of epiphysis of femur; much periosteal cartilage callus (magnifying glass); same case as fig. 602.

But micromelia is produced not only by chondrodystrophy, but also by other pathological processes. It is therefore merely a symptom and not an independent disease, though it is often erroneously spoken of in the latter sense. Shortness of the arms and legs may, with the exception of the cases resulting from aplasia of single bones, as in fig. 597, p. 1170, described by Schwendener, be produced by osteogenesis imperfecta (Vrolik, Stilling, Buday, Harbitz, lit. and others). In fig. 604, the micromelia is evident, whereas in fig. 603, some of the bones are normal in length, but thin, some are short and thickened from the callus deposited around fractures. Dwarfism may result from the disease, but not from the so-called osteogenesis imperfecta tarda (p. 1064). The process is characterized by a diminished production of bone by both marrow osteoblasts and the periosteum. The endochondral ossification, insofar as the growth and rearrangement of the cartilage is concerned, in contrast to chondrodystrophy, is practically of the normal type (Harbitz, Buday, Looser); this has also been found in our preparations (Dieterle, 1 case, Sumita, 3 cases). Thick colonies of regularly placed cartilage cells are found (fig. 602-a), the zone of hyperplastic cells is well developed (fig. 602-b), and the preparatory calcification quite extensive, or, at least, sufficient (fig. 602-c). But in his case, Eiken found insufficient preparatory calcification, and he lays particular stress on a decreased ability of the newly formed and partly abnormal

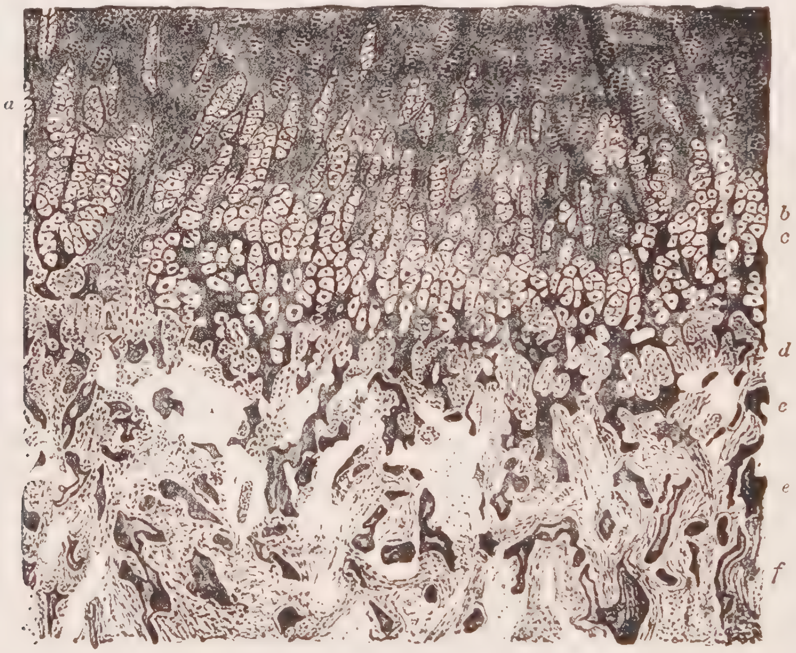


FIG. 602.—Imperfect osteogenesis; border of dia- and epiphysis; a, rows of cartilage cells; b, zone of hyperplastic cells; c, preparatory zone of calcification; d, abundant and regularly advancing marrow spaces; e, remains of calcified cartilage ground substance with sparse beginning of bone; no connected scaffolding system developed; f, marrow, very cellular, partly fibrous, rich in giant cells. Newborn girl 40 cm. long; lived for one hour. (Low power.) (Dieterle, V. A. 184, 1906.)

bony tissue to take up calcium. The progression of the marrow spaces occurs quite lawfully, and the primitive marrow spaces lie close together. But, in contrast to chondrodystrophy, the third phase of enchondral ossification is diminished; the formation of bony substance is quite diminished in the remnants of calcified cartilaginous ground substance which remains too long, and reaches far into the diaphysis; the formation of a unified and correlated system of trabeculae thus does not occur (fig. 602). The remnants of calcified cartilaginous ground substance and also the newly formed myelogenous bone trabeculae are partly removed by resorption. Thus the activity of the bone forming elements is also diminished, *i.e.*, the osteoblasts show lack of apposition in the face of vigorous (increased) resorption. The marrow may take on a fibrous, finely fibrillar, character over large areas, and Lindemann believes this is the primary cause of the entire condition; some parts are rich in spindle cells, other parts become fatty or lymphoid. Metaplastic bone formation, which is observed particularly in situations of fracture, cannot be assigned an independent role. But the fibrous marrow can be held at least partly responsible for the increased destruction process; sometimes there are numerous giant cells in the marrow. Periosteal bone formation is likewise diminished; there may be no corticalis at all. These changes all taken together produce a poor quality of bone which can be seen particularly well on cross section (fig. 601). In contrast to chondrodystrophy in which the bones become firm, in osteogenesis imperfecta they reach a high degree of fragility, hence the terms: osteopsathyrosis foetalis, recommended by Hochsinger, fragilitas ossium congenita (Klebs), osteoporosis congenita (Kundrat), etc. v. Recklinghausen recommends the name "myeloplastic malacia," because the marrow tissue predominates quantitatively over the sparse bone. Innumerable infractions and fractures may occur intrauterine and at birth (lit. concerning intrauterine fractures by Beust); these are particularly numerous in the ribs (fig. 603), which may be broken in a number of places. The diaphyses of the tubular bones are fragile, plump, and often deformed. These numerous fractures and displacements belong to micromelia, and richness of callus producing nodular thickenings at fractures is highly characteristic of osteogenesis imperfecta. Breaks are often healed at birth. (For peculiarities of the callus formation, see Eiken.) But cartilaginous callus is also very frequent in microscopic smaller or larger islands in the periosteum (fig. 601). In contrast to chondrodystrophy the bones of the skull may also be poorly developed since the diminished function of the osteoblasts is extended to the connective tissue preformed parts of the skeleton, as in fig. 604, which shows the bones of the skull as innumerable thin plates in a membranous sack. (In chondrodystrophy, on the other hand, the bones of the head are much thicker, occasionally even synostotic.) As a rule, the head is not increased in size as in chondrodystrophy (fig. 598), and synostosis in the tribasilar bone has never been observed (frequently present in chondrodystrophy). The pulling in of the root of the nose is not present; the physiognomy shows nothing characteristic. All in all, osteogenesis imperfecta, as Harbitz, among others, emphasizes, seems to be the exact opposite of chondrodystrophy, and can be differentiated quite easily (M. B. Schmidt, Looser, Dieterle, Sumita). Consequently, attempts to include osteogenesis imperfecta and chondrodystrophy under the name of fetal, or so-called fetal rickets (Michel), must be heartily discouraged.

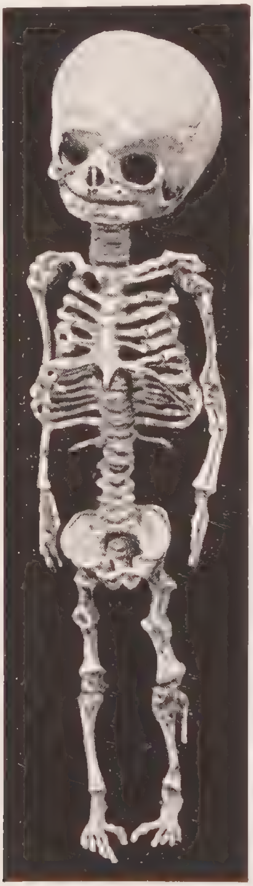


FIG. 603.

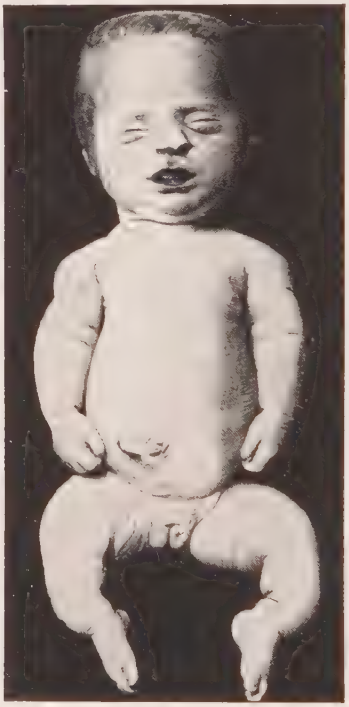


FIG. 604.

FIG. 603.—Skeleton of a case of imperfect osteogenesis with innumerable fractures and callus ormation on extremities, ribs, clavicles, etc. Skull ossified only in parts.

FIG. 604.—Micromelia in imperfect osteogenesis; many bone fractures; newborn girl; died soon after birth.

Children born with severe osteogenesis imperfecta are usually dead at birth, or die quite soon after. Those who remain living (mild cases) are the subjects of so-called osteogenesis imperfecta "tarda" (p. 1064) or idiopathic osteopsathyrosis. Dwarfism may result (p. 1182). Lit. in appendix.

Dwarfism (Nannosomia).—There occur true, false, proportionate and disproportionate dwarfs.

True Proportionate Dwarfism.—The entire body, including the surrounding soft parts fit and correspond to the well proportioned delicate bones.

v. Hansemann differentiates two groups of true dwarfs: (*a*) nannosomia primordialis, (*b*) nannosomia infantilis. In the former, the entire development of the body from the very beginning, *i.e.*, ab ovo is hindered; in (*b*) cessation of growth occurs too early, *i.e.*, in early childhood. By true dwarfism, Schwalbe understands merely an abnormally small body caused by congenital circumstances. But such a sharp differentiation of nannosomia infantilis cannot be carried out, since we do not know that it is not due to failure of anlage, even though it is manifested in later childhood (see Wieland, Dietrich).

(*a*) **Nannosomia Primordialis.**—The individuals are born abnormally small, and the development of the entire body is hindered by unknown causes. The enchondral ossification produces quantitatively less bone and cartilage in the phase of cartilaginous growth, but the destruction of cartilage and the production of bone is not hindered. The nuclei of the epiphyses develop normally. The cartilaginous columns ossify at the proper time. The skeleton, however, retains its childhood proportions throughout life. The bodies of adult, and even senile true dwarfs, vary from forty to one hundred centimeters in length. They are described as miniature editions of the genus homo. Sexual development is reached. This constitutional vegetative anomaly is hereditary; it is transmitted by the male sex, often through a number of generations. According to J. Bauer, the intelligence is about normal. The parts of the skull preformed in connective tissue are relatively large, the angle at the base of the nose is thus deepened, but this is the only disproportion. The French speak of pigmyism, but it is questionable if the comparison is apt with the pigmies of Africa (negrillos, negritos, akkas, bushman, etc.; W. Schmidt). Many also speak of nannosomia hypoplastica (Aron), and of mature dwarfs (Dietrich).

(*b*) **Nannosomia Infantilis.**—These individuals are born of normal size, but growth ceases in early youth, and the stature remains at childhood level. Ossification is diminished to high degrees. The epiphyseal columns are partly retained; those which otherwise are latest in ossifying remain permanently (Falta). Occasionally an increase in the growth in length may occur even late in life. These "child" dwarfs are possibly more frequent than the primordial, and constitute the majority of the Lilliputians in circuses, theaters, etc. The bodily proportions are regular in general, but show occasional deviations from the normal (Rossle). It is fashionable to believe that these changes are related to the internal secretory organs, which more or less regulate the growth of the body. Cases occur in which the results of these disturbances are expressed mainly in an inhibition of bone growth; in other dwarfs all the organs remain in a stage of childhood development; especially is there a failure of development of the sex organs and puberty; this, with an infantile psyche, is described as complete infantilism (J. Bauer, Anton, Brandis).

False, Proportionate or Disproportionate Dwarfism.—(*a*) A particularly interesting type of proportional false dwarfism is Paltauf's dwarfism, or hypophyseal dwarfism, earlier called hypoplastic dwarfism. Paltauf described very accurately the skeleton of a 49 year old man who was only 111 centimeters tall, but very strong; he had taken part in two wars; his bones were comparable with those of a 7 year old child, and still showed cartilaginous columns; his sella turcica was enlarged in all dimensions, so that a change was suspected in the hypophysis—see Biedl—even though Paltauf's knowledge at the time he made his observations, was insufficient to consider the function of the hypophysis in this connection. This case is the beginning of our knowledge of a particular group of dwarfs. The intact psyche is in contrast to nannosomia infantilis. This type of dwarfism also shows tendencies to sudden new growth periods at ages when normally the growth in length is completed (lit. Joachimsthal). Since microscopic cartilaginous columns persist in this condition, and also in athyreosis, it was thought that this dwarfism was of thyrogenous origin; Wagner von Jauregg believes these dwarfs are cretins, and Stoccada, agreeing with this viewpoint, confirmed the similarity of the changes in the cartilage in cretinism, athyreosis, and this type of dwarfism. Recently, Erdheim, who critically reviewed the literature concerning changes (removal) of the hypophysis (Hutchinson, Benda, Hueter, Kon), observed a case of Paltauf's dwarfism, in which a tumor of the hypophyseal duct had completely destroyed the hypophysis by pressure (the anterior lobe is important). He recognized the condition as an hypophyseal dwarfism, and called attention to the fact. It occurred in a 38 year old man, 142 centimeters tall, of infantile habitus, with hypoplasia of the genitals, and some open cartilaginous columns. Simmonds, Priesel, Nonne and others, described similar observations, but the case of E. J. Kraus is obviously more complex. Erdheim then took one step further in identifying nannosomia infantilis (v. Hansemann) with nannosomia pituitaria infantilis. The truth of this generalization has, however, not yet been demonstrated. Even though it is agreed that Paltauf's dwarfism is a nannosomia pituitaria (infantilis), *i.e.*, produced by early changes in the hypophysis, it must be admitted, nevertheless, that nannosomia pituitaria "tarda" (of Erdheim) occurring when hypophyseal changes are later in developing, is manifested as dystrophia adiposogenitalis. If the disease of the hypophysis appears after the period of growth is well begun, it no longer produces a nannosomia, and this removes a reason for not including Paltauf's dwarfism under nannosomia infantilis (v. Hansemann), nor does it justify a generalization of nannosomia infantilis as nannosomia hyperpituitarism (Sternberg). In addition, among other things, the intelligences are different; the "childhood," *i.e.*, inhibited psyche (Koch) of one, and the intact psyche of the other are sharply contrasted. But in true Paltauf's dwarfism, the hypophysis of all the internal secretory glands must be considered first. To explain the late reappearance of growth and enchondral ossification in many cases of Paltauf's dwarfism, Erdheim postulates compensatory regenerative changes in the hypophysis of which he saw indications in his cases. This necessitates the belief that the hypophysis is not completely destroyed in all cases.

(*b*) *Athyreotic or myxedematous dwarfism* is caused by more or less complete destruction of the thyroid gland; in the latter the apathetic idiotic individuals all acquire a similar typical "cretin" physiognomy. The cartilage margins remain open for life, as for example, in the well known 36 years old myxedematous idiot described by Bourneville. According to the investigations of Dieterle in athyreosis congenita and also in animal experiments, there is a highly characteristic lamellated structure of the transverse trabeculae at the diaphyseal borders of the long tubular bones which can be seen in x-ray pictures. This is the second phase of enchondral ossification (p. 1150), *i.e.*, insufficient opening of cartilage lacunae by cells of the marrow because of insufficiency of the marrow. The osteoblasts therefore produce a transverse line which is perforated like a sieve with small marrow spaces (fig. 605); this may be regarded as a symptom of inhibited growth, even though not of complete cessation, and, furthermore, the transverse lines do not inhibit growth in length when thyroid therapy is applied. Sternberg (lit.), as a contrast to nannosomia pituitaria, has described a type of proportionate hypothyreotic nannosomia, the cartilaginous margins of which are mostly open, and has classified: (*a*) infantile nannosomia in a narrower sense, which he calls nannosomia hypoplastica; (*b*) nannosomia pituitaria; (*c*) nannosomia hypothyreotica, all in the general group of nannosomia infantilis (v. Hansemann). According to the views of the author, however, it is better to exclude the cases under (*c*), *i.e.*, generally disproportioned athyreotic, or hypothyreotic dwarfism, from nannosomia infantilis (v. Hansemann);

it is probably permissible to assume that all degrees occur between very severe and mild disproportioned and proportioned forms, in which severe psychic disturbances may also occur in the proportionate form, as in Sternberg's case which cannot be differentiated from those in athyreotics (and cretins).

(*c*) *In endemic cretinism* there are various degrees of proportionate dwarfism with diminution in the formation of bone, and a persistence of the cartilaginous margins, but not usually past the twenty-fourth year of life (p. 1063, and consult Wagner v. Jauregg, Dieterle, lit.). Wagner v. Jauregg differentiates dwarfed complete cretins, dwarfed half cretins, and cretinic dwarfs without idiocy, the latter of which he identifies with Paltauf's dwarfs; see p. 1179.

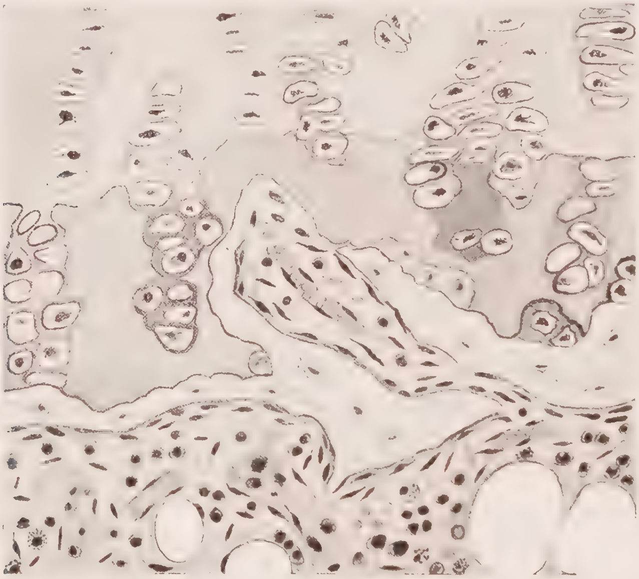


FIG. 605.—Congenital athyreosis; formation of a bony cross trabeculum (a) between calcified cartilage (b) and marrow (c); this trabeculum is penetrated by a marrow bud. (Drawing by Dieterle.) (High power.)

(*d*) In chondrodystrophy (p. 1170) there is disproportioned micromelic dwarfism; the trunk is relatively long, the members strikingly short. The epiphyseal margins disappear completely after the twentieth year; the thyroid is normal. The body itself is strong and muscular. Intelligence is practically always good. This type is related to the dwarf folk of Africa (the Wambutti, Akka), and the pygmies of the older sages, the patakes (Egyptian gods), many Spanish dwarfs immortalized by Velasquez (E. Kaufmann). A cretinoid expression of the face may or may not be present.

(*e*) Micromelian dwarfism may furthermore be caused by osteogenesis imperfecta.

(*f*) Disproportionate dwarfism is also caused by rickets; indeed, this is the most frequent cause. Short legs, particularly short thighs, and relatively normal trunks are characteristic. When these individuals are sitting down, their dwarfism is not noticed. See also shortening of the limbs as a consequence of multiple cartilaginous exostoses, p. 1198. Such anomalies of the central nervous system as microcephalia, anencephalia, hydrocephalia, porencephalia, may also produce dwarfism combined with idiocy.

Cretinism.—(The word cretin comes from Christian, and is a dialect form of Chretien.) *Cretinism* (p. 525) occurs endemically in certain situations, notably in high valleys such as in Switzerland, upper Italy, Styria; the disease is acquired in early youth, is never present at birth, is not hereditary (Siemens), is manifested by growth disturbances of the skeleton, as a consequence of which cretins become more or less dwarfed, by diminished development of the sexual organs and undeveloped function, by poor growth of hair, dry, often scaly skin, and especially by severe disturbances of the intellect. Sporadic cretinism is the name sometimes unhappily used for other diseases depending upon the removal of the function of the thyroid gland, such as (*a*) congenital myxedema, produced by thyreoaplasia (for the histological peculiarities of the diaphyseal borders, see p. 1182), and (*b*) infantile myxedema, from damage of the thyroid in childhood. The latter have also been spoken of as "complete cretins;" the better term is myxedematous idiots or myxidiots; they are a distinctly characteristic type (p. 1181). Endemic cretinism, on the contrary, is not a uniform conception, for, united in this idea, are various forms of weakness of the intellect frequently combined with goiters, and very frequently with deaf mutism, so that there is much variation in the symptoms and degrees. The physiognomy is also not uniform, and the typical "cretin physiognomy" of sporadic cretinism is not found in all endemic cases. The face is broad and plump, root of the nose deeply pulled in, forehead low, the mouth broad with thick lips through which the tongue protrudes. The bodily posture is bent, the arms hang relaxed, the gait is shuffling, uncertain and slow (reduced mobility of the hip joint). A number of cretins have goitrous parents, and some have goiters, but it is certain that some cretins have functioning thyroid gland substance (p. 525); the author examined the thyroids in two cases described by Bircher as "typical cretins;" the glands could not be differentiated from a small alveolar colloid goiter; this agrees with Kocher's theory which states "the goiter has nothing to do with cretinism as long as any healthy thyroid gland substance is retained." On the other hand, in cases with the typical bodily habitus of cretinism, Wegelin always found a seriously degenerated goiter. It is not possible to correlate sporadic thyrogenous with endemic cretinism, with the idea in mind that both are caused by removal of the function of the thyroid (Ewald, Dieterle, Scholz), especially not because implantation of thyroid gland or the administration of its preparations do not influence the most important point in endemic cretinism, viz., the psyche (Scholz and others); the observed favorable influence of thyroid preparations on the cretin skeleton (increase of growth in size), is not specific, but depends upon a rapid deposit of calcium salts in the growth lines in much the same manner as the same preparations produce it in the normal skeleton (Eug. Bircher). The definition of Scholz seems better: "endemic cretinism is a strumous change of the thyroid occurring in inhabitants of certain territories, caused by unknown conditions, and accompanied by cerebral damage." In the Pathological Institute of Basel we arrived at a similar conclusion (Dieterle, lit.). For the hypothecated causes of endemic cretinism, see p. 525, also Diviak, Wagner v. Jauregg, and below.

Virchow thought he could demonstrate a premature synostosis of the sphenobasilary synchondrosis of the skull as a consequence of increased ossification; others have taken this finding to be the general rule for the skull and other bones of cretins, an error which helped in perpetuating the erroneous idea of chondrodystrophy being fetal cretinism (see for example, Ewald who still believes in this idea; p. 1172). The investigations of Langhans, Rob. v. Wyss, Scholz and others, have, however, shown that the conditions are diametrically opposed; a premature synostosis of any cartilaginous margins has never been shown in any notorious cretin; the epiphyseal surfaces, on the contrary, remain open long after the normal time, and the shortening of the skeleton, the pars basilaris occipitis and the sphenoid bone (Stoccada), is due to an insufficiency of the marrow, *i.e.*, in breaking open the cartilage lacunae in the second phase of enchondral ossification. Even in the forty-fifth year of life, Langhans found remnants of these margins and described the transverse trabeculae at the diaphyseal borders of athyreotics as indicated on p. 1181. Stoccada and Wegelin also called attention to the similarities of endemic cretinism and athyreosis. According to the former, the synchondrosis sphenooccipitalis persists even longer than the remaining cartilaginous joints. Roentgen ray examinations (Hofmeister, Rob. v. Wyss, Scholz and particularly Eug. Bircher), in the living showed that the difference in the ossification (inhibition of ossification of the cartilaginous skeleton), in comparison to the normal, persists for only a few years, and that after the twenty-fifth year, it is demonstrable macroscopically in only exceptional cases. This condition of the skeleton of cretins is different from the skeleton of myxedematous and infantile dwarfs in which the joints persist throughout life, but fig. 606 shows many similarities. J. Bauer emphasizes that the irregularity of the growth inhibition, the incomplete closure of the joints, and isolated differences in epiphyseal joints, cannot be correlated with the assumption of a purely thyrogenous genesis. The most possible is participation of the thyroid in disturbances of the general endocrine glands. The facts that cretins are not influenced by thyroid preparations in contrast to other thyrogenous conditions, that their skin can be lifted up in folds in contrast to myxedema, also speak against a purely thyrogenous

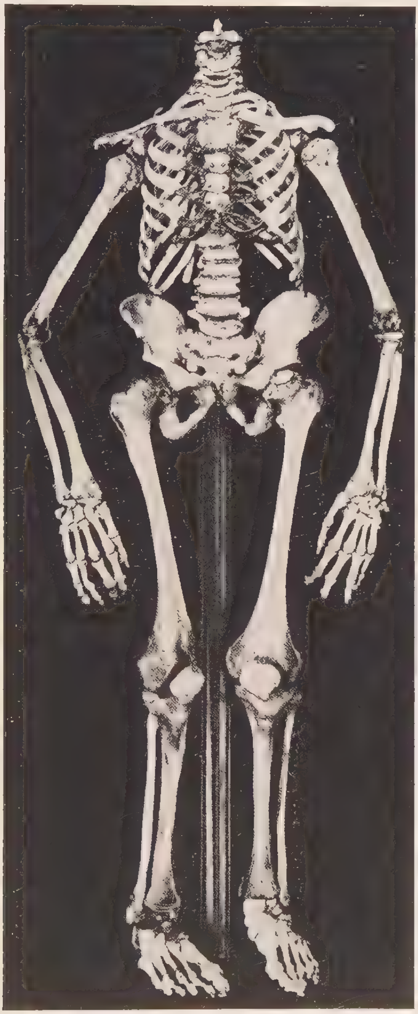


FIG. 606.—Skeleton of a cretin 58 years old; cretin dwarf (body length 120 cm.) described by His sen. in V. A. 22, 1861, and mentioned in text; the head is in Berlin. Femur as a whole well built and straight, partly open lower epiphyseal line both in femur and humerus.

nature. The astonishing demonstration of Erdheim that Paltauf dwarfism is of pituitary nature, and that the microscopic epiphyseal border agrees with that of athyreosis and cretinism, (p. 1180), argues caution when speaking of etiological factors. According to Langhans, the bones of cretins are well proportioned, and the minority (Scholz), are graceful rather than plump (de Quervain). The skeleton in the Basle collection described by His senior, has graceful bones; in this 58 year old individual, the joints between the basilar bone and sphenoid body were still cartilaginous (lit. Weygandt, Scholz, Eug. Bircher; see also Lawen). In two cases, Zieleniewska-Stefanoff saw persistence of the youthful condition of the larynx and the cartilages of the ribs. Concerning the bone marrow of cretins (many foci of lymphocytes and follicles, many eosinophilic cells), see Stoccada, and compare Kind. Concerning tooth anomalies in cretins, see Kranz.

Gigantism, Macrosomia.—We differentiate general and partial gigantism. Among the former are individuals of a height of about two meters and upward to 2.83 meters.

The etiology of generalized gigantism (macrosomia), is obscure, but it is described as an hypertrophy of congenital anlage. The condition is not hereditary; traumata are considered helping factors by giving an external stimulus to the increased growth tendency inherent in the anlage. The minority are "normal" giants (simple gigantism), and show no striking vegetative changes. The majority are "pathological," among which are the plump acromegalic giants with changes occurring in the hypophysis cerebri; others are called gigantism infantilis, the so-called tall type (175 to 200 centimeters and more). In the disproportionate long-legged giants of the latter kind, the infantile stage of the genitals and the lack of secondary sex manifestations are characteristic; these are believed due possibly to congenital hypoplasia of the sex glands and thus they are called eunuchoids (Tandler and Grosz, Saenger, Josefson and Sundquist, Voelkel). Psychic defects are frequent (infantile psyche; actually, however, merely a failure of development of manhood, Borchardt); the cartilaginous joints remain open as in nannosomia infantilis. The latter, and the striking elongation of the legs (the pelvis remains like that of a child) with the atrophy or hypoplasia of the genitals, is common to giants and eunuchs, *i.e.*, in whom castration has been done early and in whom, among other things, there is enlargement of the hypophysis (p. 1150), (the thyroid is small), which is said to be responsible for the increased growth in length; the other castrate type is corpulent, adipose, edematous (similar to dystrophia-adiposo-genitalis caused by hypophyseal trouble). Libido and facultas coeundi are not extinguished in those castrated late (Tandler). (In those castrated later, the sutures remain open longer, Sellheim.) Exceptionally, however, there are cases of gigantism with increased ossification, early closure of the epiphyseal joints and general early development, especially of the genitals (see Redlich, and under epiphysis cerebri). Giants usually have small heads. The skeleton is not as well proportioned as that of normal individuals of ordinary size (Langer). The hips are exceptionally broad. The individual bones are also poorly proportioned, plump, covered with exostoses, bowed; occasionally they show signs of chronic atrophy, have a wide-meshed spongiosa, are abnormally brittle, malacic, and the giant body may collapse from failure of support of its framework. Just as his skeleton is usually of poor internal structure, the giant himself is usually a weakling; his musculature is poor and weak in relation to his bodily size. Giants usually do not live to old age. Partial gigantism is an idiopathic, probably congenital anlage hypertrophy of a part of the body, which is, however, not simply quantitative, but with hyperplastic and dystrophic disturbances of a specific qualitative nature (Peiser). The frequently observed inhibitions and excess of structures such as hyperdactylia, syndactylia, naevi, etc., also point to a congenital anlage defect. Traumata, (the kick of a horse in the face in the case of Buhl), and progressive or frequently recurring inflammations are said to have an etiological role. As far as the bones are concerned, the hypertrophies are met in isolated toes and fingers, particularly the middle finger (lit. by Wittelshofer, M. B. Schmidt, Hofmann, Wieland, Flinker, Hinterstoisser, lit., W. Fischer), occasionally in the roof of the skull or one side of the face (the rare hemihypertrophia faciei of syringomyelia described by Stahle, lit.). Usually the fatty tissue is also hypertrophic (lit. Pick). The hypertrophic conditions spoken of as leontiasis ossea, ostitis deformans (p. 1107), and osteoarthropathy (p. 1115) should be differentiated from gigantism.

Acromegaly (fig. 550, p. 1114) may lead to "normal" gigantism, and according to Sternberg, 40% of all giants are acromegalics. Thus there may be differentiated, simple (Langer's "normal"), and acromegalic giants (Langer's "pathological" class). But that acromegaly and gigantism are so closely related that we may speak of gigantism as "acromegaly of the growth period," and acromegaly itself as "late gigantism," cannot be admitted, a point which M. Sternberg stresses particularly (Thomas, lit.). But the disposition of gigantism to acromegalic disease is undoubted. Acromegaly which appears after the growth period need not be coincident with gigantism (Exner).

The following do not belong to actual gigantism: the "fat ladies" of the sideshows; this is an internal secretory disturbance; 2. the so-called giant children, which arrive in the world at the normal time (280 days), or as late births in which pregnancy lasts too long a period (even 300 to

340 days), and in which there is an abnormally rapid intrauterine growth of the child. In these cases, many speak of fetal gigantism, others of primary enlargement of the ovum (Fuchs). Weights of 6,000 grams and more occur, (11,300 grams in a child 76 centimeters long, see Ahlfeld; the circumference of the head instead of 34½ cms. increases to 37 to 41 centimeters; see Zangemeister). See Kustner, v. Winckel, Fuchs, lit., Ciulla, lit.

Increased growth in length (elongation) of the bones of extremities, particularly the femur and tibia, usually with thickenings (hyperostoses), may occur: (*a*) following irritation of the epiphyseal cartilage in young individuals. By the introduction of splints of ivory in the epiphyses of young animals an enlargement and elongation of the bones have been produced experimentally even though not constantly. (*b*) Various diseases and injuries of the diaphyses, and the soft parts covering them may produce an elongation of one or more centimeters. There might be mentioned: osteomyelitis (simple, chronic, or fibrous, or gummatous), necrosis of the diaphyses, fractures of the bones, leg ulcers during the growth period, genuine diffuse phlebectasia (Sontag), intramuscular suppuration, ectasy of vessels (varix aneurysmaticus), neurofibromatosis, etc., (Milner, Perthes). Elongation of a neighboring bone, itself not diseased, has even occurred. (*c*) Changes in the joints may also lead to elongation of the bones; this has been observed occasionally in tumor albus (lit. Wartmann), in the presence of joint mice, and after a knee joint contracture. (Lit. by M. B. Schmidt.)

Premature Synostoses.—If ossification takes place too early along the sutures (syndesmoses), or along the synchondroses, the growth of that particular part is ended. If it occurs along a suture of the skull, the growth ends at right angles to the suture which has become synostotic, (for example, in synostosis of the sagittal suture, the skull does not become sufficiently broad). The skull dilates in other directions as compensation, so that its capacity is not much reduced if merely isolated sutures are prematurely ossified. On p. 1171 was discussed premature synostosis of the intersphenoidal and sphenobasilary synchondroses which produces shortening of the base of the skull. In many cases of microcephalia (abnormal smallness of the skull), there is no change in the sutures; in others, some, or even all, are prematurely closed; thus the brain, influenced by changes in the skull, is usually poorly developed; even complete cessation may be caused by microcephalia. Macrocephalia may be caused, among other things, by the sutures remaining open too long.

A steep pelvis (the narrow pelvis of Naegele) is formed by premature synostosis of the sacroiliac synchondrosis of one side (but also by defects, deformities, hypoplasias of one ala of the sacrum, inasmuch as the involved side ceases in its growth, and the os pubis is pushed toward the opposite side. If the synostosis or hypoplasia is bilateral, the transversely narrow pelvis results (see in the entrance to the pelvis), the straight measurement of which is, however, not changed (lit. Breus-Kolisko; see also Bayer).

Pathological Deformities of the Skull.—According to Virchow, most deformities of the skull can be explained by premature obliteration of the sutures, local disturbances in growth, and compensatory hypertrophies. But according to the investigations of Thoma, which disagree with Virchow's in many respects, premature synostoses influence the shape of the skull only when they occur during fetal life or in the first two years of life. It can no longer occur after this time, since appositional marginal growth is no longer demonstrable; the flat growth of the roof of the skull is then chiefly interstitial.

Virchow's pathological skull shapes are as follows:

1. **Simple macrocephalia:**
   (*a*) Hydrocephalia. (*b*) Kephalones, large heads.
2. **Simple microcephalia,** nannocephalia, dwarf head. (Final synostosis of all sutures.)
3. **Dolichocephalia,** (elongated head).
   1. Of the upper middle synostosis:
      - (*a*) Simple dolichocephalia, elongated head (synostosis of the sagittal suture).
      - (*b*) Sphenocephalia, wedge shaped head (synostosis of the sagittal suture; the region of the large fontanelle compensatorially developed).
   2. The lower lateral synostosis:
      - (*a*) Leptocephalia, small head (synostosis of the frontal and sphenoidal bone).
      - (*b*) Klinocephalia, saddle head (synostosis of the parietal, sphenoidal and temporal bones).
   3. Fetal synostosis of the halves of the frontal bone: Trigonocephalia, the forehead is diminished in size, narrowed like a keel, viewed from above, the head is three-cornered.
4. **Brachycephalia,** short head:
   1. Posterior synostosis:
      - (*a*) Pachycephalia, thick head (synostosis of the temporal bones with the tabular part of the occipital bone); the posterior part of the head is broad.
      - (*b*) Oxycephalia, the pointed, sugar-loaf head (synostosis of the parietal with the occipital and temporal and compensatory

development of the anterior fontanelle region; the head is broad from the front.

2. The upper anterior and lateral synostosis:
    (*a*) Platycephalia, flat head (extensive synostosis of the frontal and parietal bones).
    (*b*) Trochocephalia, round head (partial synostosis of the frontal and parietal bones in the middle of the half of the coronary suture).
    (*c*) Plagiocephalia, oblique head (unilateral synostosis of the frontal and parietal bones, *i.e.*, of the coronary suture, compensatory elongation of the other half of the skull).
3. Lower, middle synostosis:
    Simple brachycephalia (synostosis of the base and sphenoid body).

A variety characterized by partial premature ossification of the coronary suture and secondary synostosis of the sagittal suture (mixed form of brachycephalia and dolichocephalia, see Rieping, lit.), is shown in the congenital and hereditary turricephalus produced by variations in the germinal cells; a displacement of the primary centers of ossification of the frontal and parietal bones (the tubercles), to the coronary suture, is followed by a premature synostosis of these sutures; the apex of the abnormally high skull begins just behind the large fontanelle, and is formed by a crista, which represents the ossified sagittal suture. From this crista the parietal bones fall off abruptly. The forehead is high and steep, the orbits high and flat. The bulbi may be pushed forward because of a frontal position of the large sphenoidal wings, whereby the orbits are shortened. The gums are small and high. Atrophy of the optic nerves may follow (Oberwarth, Bullinger, Mehner). Dorfmann believes the intracranial pressure is increased, and recommends trephining (see Schloffer, Herzog, Strebel); Meltzer and Goldstein think of a fetal meningitis, which later leads to optic atrophy by a new exacerbation of the hydrocephalus. According to Strebel, on the other hand, the brain growing in a too narrow, prematurely synostotic skull is the cause of the increase in intracranial pressure; it models the impressions, broadens the sinus, "bulges the emissary foramina to almost trephine openings," and compromises the inner plate. Differential diagnosis by Vaternahm.

Dysostosis cleidocranialis (P. Marie, Sainton), is an hereditary germinal anomaly of the bony system, showing the following changes in the skull: brachy- and platycephalia, marked development of the eminence, pulling in of the lower parts of the lateral walls, relative predominance of the cerebral in contrast to the face skeleton, a steep profile of the face, poor development of the jaw apparatus, the teeth, etc. The most characteristic point is the persistence of the sutures and fontanelles, even into senility (Scheuthauer). Raubitschek saw normal clavicles with fissure-like clefts in the sternum, but the clavicles may be the only bones involved (Preleitner). This developmental anomaly may be familial (lit. J. Bauer). For other malformations involving the bony system such as cleft pelvis, without changes in the soft parts, general hypoplasia of the skeleton, etc., pointing to a general dysostosis, see Breus-Kolisko, Paltauf. In the shoulder girdle, there are defects of the clavicles, or a kind of pseudarthrotic solution of continuity or a bowing of these bones, observed with growth inhibition of the shoulder blades (Hultkrantz, lit., see also Fitzwilliams, lit., Apert).

Tumors of the Bones

[For comparison with the classification given below, see the Registry of Bone Tumors of the American College of Surgeons. Codman, E. A., Surg., Gyn. & Obst., 34: 335: 1922; 38: 712: 1924; Am. J. Roent. & Rad. Therap., 13: 105: 1925.—*Translator.*] All benign and malignant primary bone tumors are of connective tissue origin; they arise from the periosteum, the bone marrow, or the cartilage. If a number of different structures are represented in a single growth, it is known as a mixed tumor.

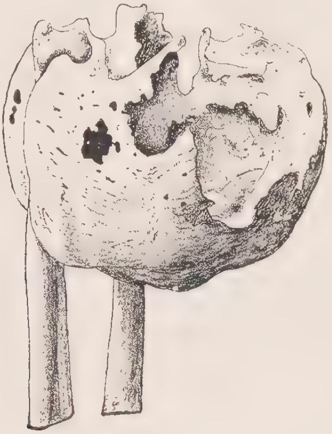


FIG. 607.—Myelogenous giant cell sarcoma, larger than a fist with bone capsule. Capsule sarcoma of lower end of right radius; to left, the ulna which lies in a channel of the bone capsule; supposed to be present 8 years; from a seamstress 35 years of age.

According to the situation in the bone from which the tumor arises, we differentiate: peripheral tumors, usually from the periosteum, less commonly from the peripheral cortical layers, and central or endosteal tumors, arising from the spongiosa or the marrow cavity. If a periosteal tumor is benign, it usually comes from the internal layer of the periosteum and is covered by the external layer; malignant periosteal tumors, on the other hand, soon grow through the periosteum; occasionally they arise from the external layers. Central tumors, usually of myelogenous origin, produce circumscribed or diffuse growths, which destroy the surrounding bone by resorption, resulting in irregular cavities in which the tumor or tissue lies; this resorption is partly in the form of lacunar disappearance with Howship's resorption lacunae and the presence of osteoclasts (giant cells). On the other hand, these tumors sometimes tend to produce bone; thus internally, an endosteal tumor mass may be surrounded by sclerotic tissue. If the tumor invades the periosteum, new layers of bone are produced externally, but since the new layers are continually being resorbed again as the tumor grows, the bone becomes inflated, so to speak, in a way similar to that described

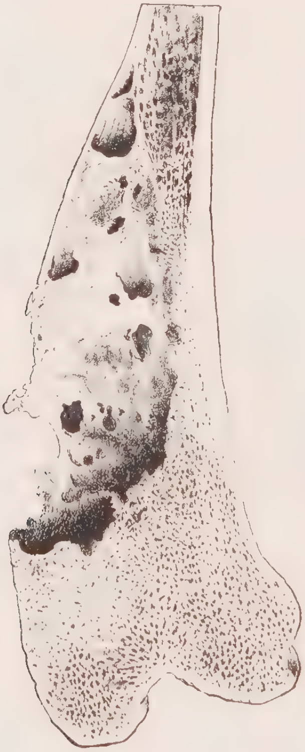


FIG. 608.

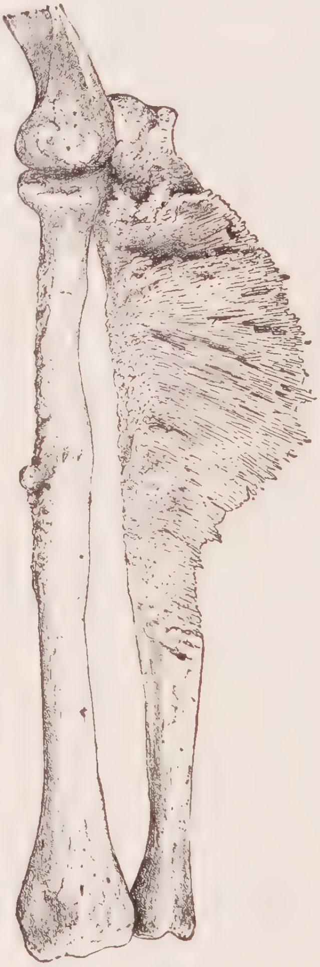


FIG. 609.

FIG. 608.—Skeleton of a large cell myelogenous sarcoma of femur, posterior half; capsule formations in upper part of cavity which was filled by tumor tissue. The shell is thickly sclerotic inside. Robust man, 40 years old. Amputation; ½ nat. size.

FIG. 609.—Osteoid sarcoma of left ulna. The skeleton, *i.e.*, the bony root after maceration of the outer, soft tumor mass. Atrophy and osteophytes on outside of radius.

under tuberculous spina ventosa (fig. 562). The tumor is thus surrounded by a bony shell, which is more or less completely closed (figs. 607 and 608). The shell is more complete, the slower the growth of the central tumor, and the more complete the retention of periosteum. In rapidly growing tumors, the shell cannot close because the tumor masses soon penetrate and destroy the periosteum, which is not replaced. The tumor then invades the neighboring soft parts without hindrance. The central, usually myelogenous, sarcomas are especially adapted to produce a shell and may develop even in the thinnest bones, as for example, the fibula, where they have been known to reach the size of fists or men's heads (shell sarcomas). But shell formation may also occur in peripheral, usually periosteal, sarcomas. Fig. 610 shows this in a rare sarcoma of the left temporal bone.

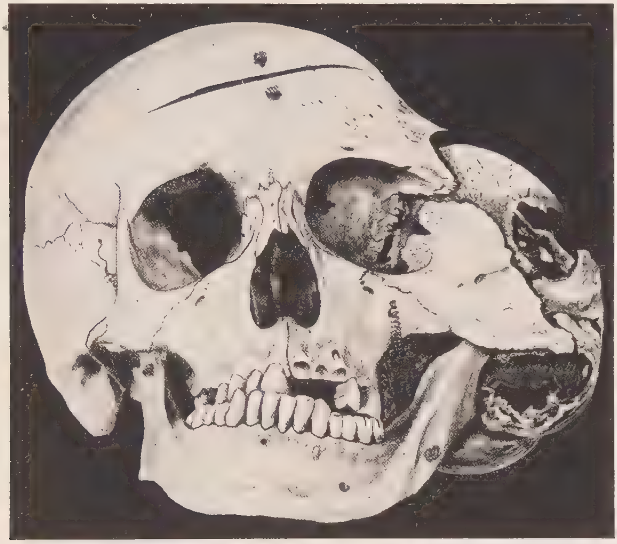


FIG. 610.—Peripheral capsule sarcoma of the left temporal bone; marked deformity of lower jaw, left malar bone and orbital bones; ⅓ nat. size.

Large shell tumors contain, as a rule, an internal bony framework in addition; the trabeculae of this structure, which insert into the inner surface of the shell, are produced by the tumor substance itself, and not by periosteum. Often, however, the formation of bone is incomplete in many situations, and there is then found an irregularly calcified osteoid. In macerated preparations the skeleton of a shell tumor may therefore be quite fragile.

In other cases, a central tumor comes from the marrow and partly destroys the cortex, while in other situations, it grows through the Haversian canals without destroying the cortex, until it appears externally, as perhaps an enormous peripheral tumor; in such cases, it is difficult to determine whether they are primarily peripheral or primarily central tumors.

A striking peculiarity of most primary tumors arising in bone, and some secondary tumors (carcinomas) is the tendency of the tumor tissue itself to produce bone, or to stimulate a vigorous production of bone. In many, as for example, those which begin as cartilaginous growths (enchondromas), this ossifying tendency may lead to complete bony transformation. Sarcomas also, particularly the periosteal varieties, may ossify over large areas, so that the term osteosarcoma is justified. Occasionally the bone production is incomplete, osteoid. Large parts of a soft tumor may be infiltrated with newly formed bone tissue. In other cases, merely parts of the tumor are ossified or become osteoid; this is particularly true of sarcomas, thus, for example, an ossified pedicle may be formed, (fig. 611), or radiating delicate needles, leaves or strands, often in groups, and often hollow like fine tubes, composed of bone (fig. 609).

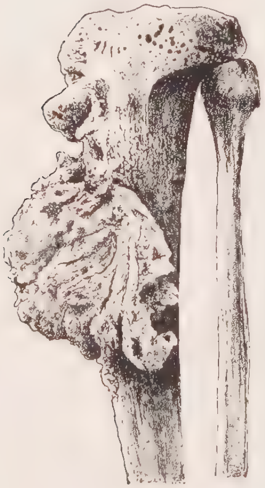


FIG. 611.

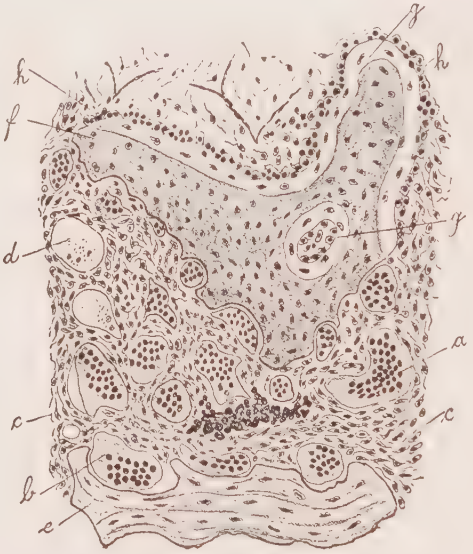


FIG. 612.

FIG. 611.—Skeleton, or bony framework, finely porous, of a large globular periosteal osteochondro-sarcoma of left tibia after maceration of the larger soft tumor mass. The tumor invades the medullary cavity; from a girl 10 years old.

FIG. 612.—Bone absorption and new bone formation in giant cell osteo-fibro-sarcoma of ulna. a, giant cell; b, giant cell in a Howship's lacuna (osteoclast); c, sarcoma tissue, fibrous and spindle and giant cells. In specimen center brown blood pigment; d, blood vessel; e, old bone trabeculum; f, new formed bone by osteoblasts g; h, bone edge not yet calcified (osteoid). (High power.)

Ossification occurs by way of osteoblasts as well as by metaplasia from a fibrous, or cartilaginous, or even a richly cellular sarcomatous tissue; the preceding cells may be enclosed in cavities and become bone corpuscles, while the ground substance is osteoid, which becomes bony by taking up calcium. Metaplastic bone is of poor architecture, rich in irregularly distributed bone corpuscles, and is not lamellated (fig. 612-f), but lamellae of bone may be laid down by osteoblasts on bony trabeculae produced by metaplasia (fig. 612-g).

Calcification or petrifaction of the ground substance, particularly in sarcomas, must not be mistaken for ossification.

What is known of the etiology of bone tumors will be discussed in more detail under the individual forms. In general, it might be remarked that anomalies in the development of the skeleton (particularly in chondromas and osteomas), trauma, (particularly in sarcomas), are of some importance.

The Individual Forms of Bone Tumors

Osteomas.—Circumscribed tumors composed of bone tissue are called osteomas; if they are raised above the surface of the bone, they are called exostoses; if they are internal in spongy bones, they are called enostoses; the latter are rare, and are met in the roof of the skull, in the bones (lower jaw) and cavities of the face, (usually coming from the cribriform plate). The upper jaw, cribriform plate, and the sinuses may be dilated and perforated, and the tumor appear in the orbit or in the skull cavity. As emphasized before, many inflammatory new growths can be differentiated from actual bone tumors only with the greatest difficulty. Osteophyte is the general name for periosteal new bone formations; they are characterized by many and broad Haversian spaces. An exostosis is smaller than an osteophyte, which becomes prominent like a tumor, and often appears without demonstrable cause, as for example, without inflammation. A diffuse massive increase in a bone is called hyperostosis; there do occur, however, circumscribed hyperostoses, which can be differentiated from exostoses merely because they are less circumscribed and less prominent on the surface of the bones.

According to the structure, there are differentiated: exostosis eburnea, a compact, stony hard, ivory-like tumor, composed of bony lamellae, often without a trace of marrow, and allowing the recognition of few, or practically no Haversian canals; exostoses spongiosa are porous, and marrow spaces and bony tissue are about equally divided; exostoses medullaris contain very broad marrow spaces. The marrow in exostoses behaves in general as the remainder of the bone marrow (p. 286).

According to the genesis, there are differentiated: (*a*) cartilaginous or epiphyseal, and (*b*) connective tissue preformed, *i.e.*, periosteal and so-called tendonous exostoses.

(*a*) **Exostosis Cartilaginea (Cooper), Ecchondrosis Ossificans (Virchow).**—An exostosis cartilaginea is a tumor situated immovably upon a bone, of rounded, irregular exterior, composed internally of spongy bone, its outer layers of compacta, with a hyalin cartilaginous layer as a covering of its surface. The tumor enlarges by cartilaginous growth and enchondral ossification, as well as by growth of the periost-perichondrium. In the ossification of ecchondroses, there are vessels which lie in a tender fibro-cellular marrow tissue, and which invade prepared calcified cartilage; the deposit of lamellated bone by osteoblasts follows, but frequently in very irregular forms, in spots or perhaps in layers of varying thickness; larger pieces of prepared opened cartilage may at first remain free from deposits. These exostoses grow only on parts of the skeleton which were previously cartilaginous. The most important points of origin are the, epiphyseal cartilages (Virchow, v. Recklinghausen), from which the tumors appear as ossifying outgrowths (ecchondrosis ossificans, Virchow), or as displaced parts of these from the cartilaginous grooves, or from the edges of the joint surface. According to Virchow, these cartilaginous exostoses depend on a developmental disturbance in the bones, and multiple cartilaginous exostoses are genetically closely related to enchondromas. which come from islands of cartilage displaced from the growth cartilage; in enchondromas, the islands of cartilage lie in the spongiosa; in the other type, (exost. cart.), they are subcortical, and quite early, C. O. Weber described multiple exostoses as coexistent with very large multiple

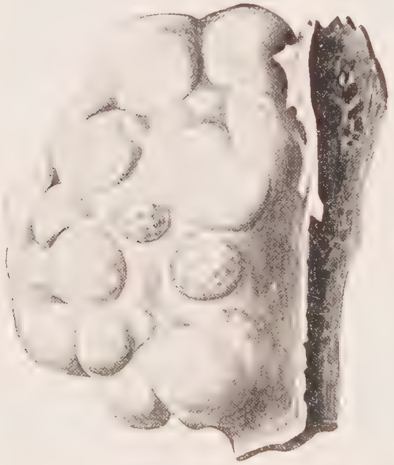


Fig. 613.—Ecchondrosis ossificans of upper end of diaphysis of humerus, externally hyalin cartilage; within similar conditions as in cross section, fig. 614. The ivory hard bands form groups; boy of 12; 5/6 nat. size.

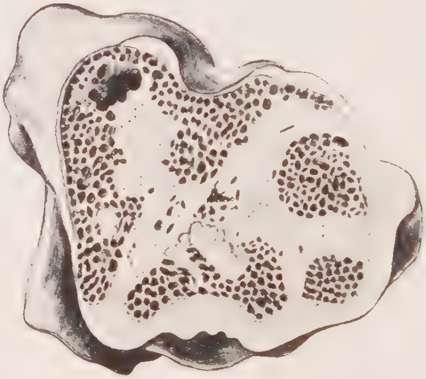
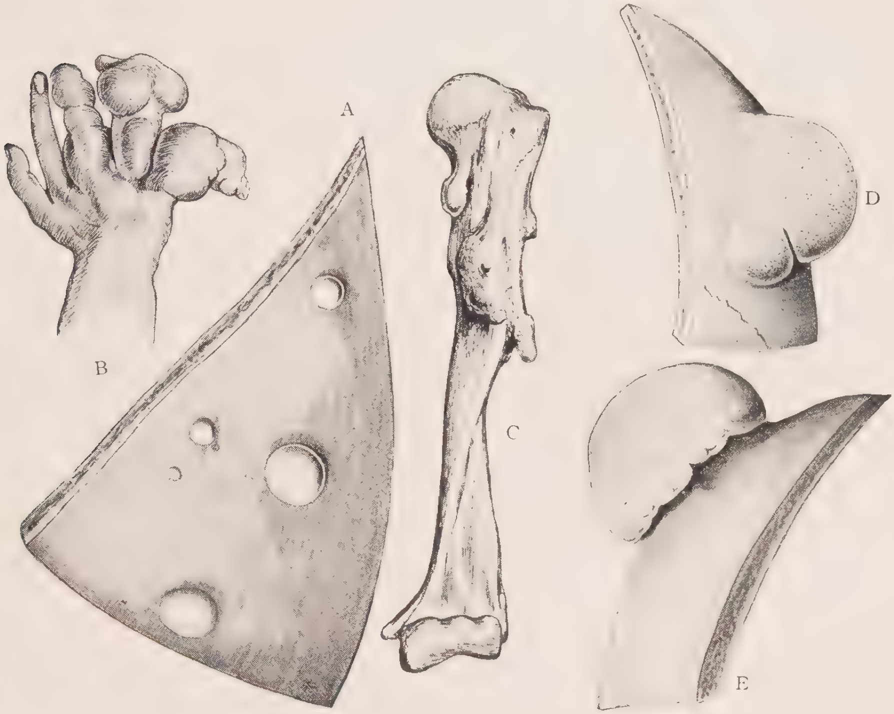


Fig. 614.—Ecchondrosis ossificans of upper end of l. fibula. Cross section showing spongy bone containing ivory-hard bands of calcified cartilage; a small island of blue white cartilage near circumference of the cartilaginous coating; man 24 years old; 5/6 nat. size.

enchondromas. In a case described by Chiari, the skeleton of a 19 year old individual showed about 1000 exostoses, and in many furrows of the surface, showed small, to hazel nut size islands of cartilage. E. Muller (comprehensive lit.), believes they arise from intraperichondral and intraperiosteal cartilage islands, the formation of which depends upon a chondro-productive constitutional anomaly of the perichondrium and the periosteum. Following the lead of Virchow and Volkmann, Flinker hypothecates general etiological relationship to rickets. They occur chiefly in younger individuals during their growth period, and are occasionally multiple (exostosis cartilaginea multiplex). Inheritability has been noted, often through a number of generations (Prince, Drescher, Jungmann, Pels-Leusden, lit., and others). Erdberg, who saw 7 cases in one family, hypothecates relationships to aplastic and regressive changes in the thyroid. The long bones are preferred, but exostoses also occur in the bones of the hands and feet, the vertebral column, the ribs (Jager, lit.), the shoulder blades and the pelvis. They produce Kilian's pelvis, acantho-pelvis, pelvis spinosa (lit. by Breus and Kolisko), *i.e.*, the carti-



FIGS. 615–619.—A. Ivory-like exostoses on frontal bone. B. Multiple chondromas (enchondromas) of fingers of right hand (after Cornil and Ranvier); C. Exostoses on humerus at insertion of deltoid muscle, so-called "drill" bone, after Nelaton. D. Exostosis spongiosa at right of coronary suture, encroaching on r. lower angle of parietal bone; ⅔ nat. size. E. Exostosis eburnea of l. parietal bone from an old man; ⅔ nat. size.

laginous spinous exostoses appear in the region of the pelvic joints, and extend as points or nodules up to the size of a man's head into the cavity of the pelvis. Multiple cartilaginous exostoses become stationary when the general body growth ceases; this is different from the status of true tumors of similar structure (enchondroma), and relates them to hyperplastic processes; even regressive changes occur in them (Hartmann). Multiple cartilaginous exostoses and enchondromas frequently lead to growth disturbances of the bone, such as shortening, especially of the ulna and tibia, and to disproportions (lit. by v. Haberer). It may result in a general smallness of the entire individual (consult the review by Breus and Kolisko, lit.). Other anomalies such as telangiectasias, lipomas, pigment spots, etc., may be coincident (Jenny). Chiari saw sarcomatous transformation, but in contrast to enchondromas, it is rare (Mosenthin, Lawen); compare p. 1205.

(*b*) **Exostosis Fibrosa.**—Among these connective tissue preformed osteomas which are covered only by connective tissue and not by cartilage, there may be differentiated: those which arise from the periosteum to which they are tightly adherent (immobile periosteal exostosis or cortical osteomas), and those which arise from the external parts of the periosteum and are movable (movable periosteal exostoses). The name parosteal osteoma is used when an osteoma forms in the neighborhood of the bone either from the breaking loose of an exostosis, or from a piece of detached periosteum, and discontinuous osteoma, when osteomas develop in the fascias, tendons, ligaments and muscles distant from bones. Continuous fascial, tendonous, ligamentous, or intramuscular osteomas are connected to the bones, and as comb-like or thorn-like structures, are no doubt, merely very long exostoses. Heterotopic osteomas are those which appear in situations where no bone is normally present; they are produced by ossification of a cartilaginous matrix, or come from the connective tissue of the soft parts either by metaplasia or neoplasia from misplaced osteoblasts. Such heterotopic bone formation is seen in the meninges, in the brain itself, in the lungs, in the trachea, in the parotid gland, in the choroidea and the sclera, in the skin of older people as well as in other situations, such as inflammatory cicatricial connective tissue structures (see under pleural bones, p. 488). These bony formations in the connective tissue of the muscles distant from bones, are looked upon as myopathic, *i.e.*, as a product of myositis ossificans (see under this disease), and must be considered with the heteroplastic osteomas. Those which are continuous, often multiple, and situated at the site of insertion of muscles, are called muscle insertion exostoses. These are seen, for example, along the linea aspera femoris, and in situations where normal protuberances and tuberosities are present on the bones (fig. 618, and under muscles). The origin of these exostoses is believed due to irritation of the periosteum. They usually occur in younger individuals; their sites of preference are on the inner sides of the thigh, and the upper third of the arm. The x-ray has detected frequent and typical calcaneum exostoses, the so-called spurs, on the middle tuberosity of the calcaneum, for which the most varied etiological factors have been held responsible such as arteriosclerosis, gonorrhea, etc., (lit. Rolly, H. Virchow, Appelt and others).

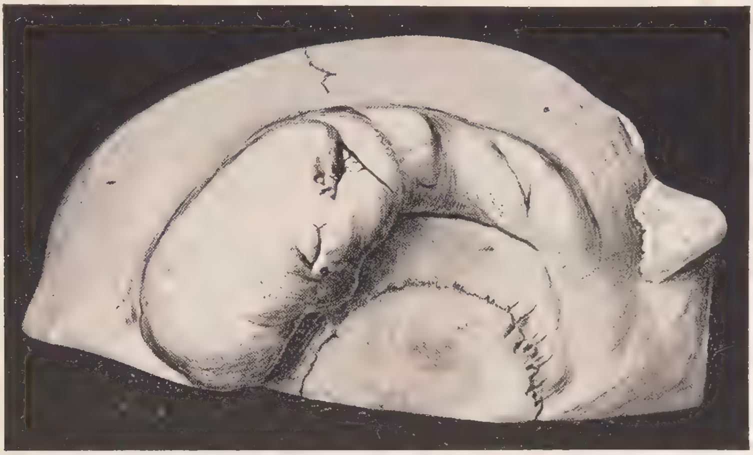


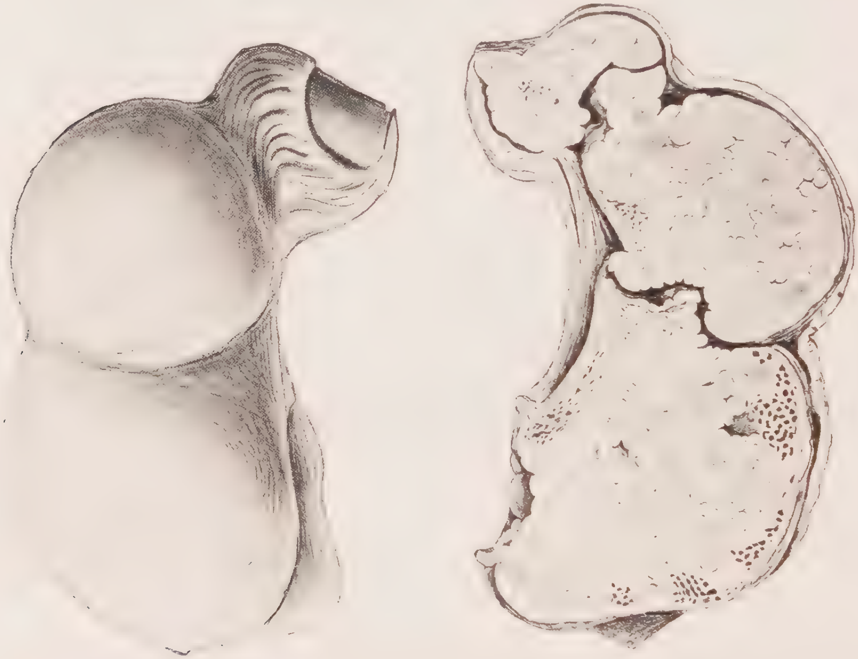
Fig. 620.—Exostoses of skull. Large kidney-shaped exostoses extending over coronary suture and from l. parietal bone to frontal bone. A pyramid-shaped exostosis and a small flat one behind the larger.

Cortical osteomas are frequent in the roof of the skull, as small flat, or button-shaped, occasionally pedunculated, sometimes multiple, ivory-hard thickenings of the external table, particularly in the frontal and the parietal bones (fig. 615-a). More rarely, they are larger, broad, spongy, or ivory-hard, rounded bony outgrowths (fig. E. p. 1197); larger ones as illustrated fig. 620, are kidney-shaped, and still larger ones as big as a fist, are quite rare (Luxembourg, lit.). According to Arnold, the goose egg-size, ivory-hard, so-called cavity osteomas of the pneumatic accessory sinuses are also exostoses. If they become separated from the wall from atrophy of their pedicles, they are called dead osteomas (Tillmanns).

A bone tumor (osteoma fracturae), produced by a luxuriant callus (p. 1088), occurs particularly often in the flat bones, *i.e.*, the shoulder blades, the pelvis, but occasionally also in the long tubular bones in spinous or branched forms (fig. 537, p. 1088).

The exostosis subungualis of the large toe is of considerable practical importance. A small spongy bony tumor appears directly under the nail or along its edges; the nail is lifted upward; it disappears from pressure so that the surface of the bony nodule becomes ulcerated. The tumor then becomes very painful. It prefers younger individuals.

Fibromas of the Bones.—In general they are rare. They appear most frequently in the bones of the mouth and surrounding the nasal cavities (jaw, particularly lower jaw), where they arise from the periosteum or centrally, and bulge out the jaw (p. 592). See also under naso-pharyngeal polyps, p. 303, and epulis fibromatosa, p. 573. The fibromas of the periosteum are often very vascular, so that on cross section they appear somewhat like a corpus cavernosum (telangiectatic fibroma). Transitions to sarcoma occur in the naso-pharyngeal fibromas; among these a particular form appears in which there is extraordinary development of wide blood vessels surrounded by sarcomatous collars (telangiectatic angio-sarcoma). As in all bone tumors, bony trabeculae are occasionally developed in the tumor tissue (fibroma ossificans). Consult fibroma under ostitis and osteomyelitis fibrosa, p. 1107.



Figs. 621 and 622.—Finger with central enchondromas from outside. The same finger cut lengthwise. Joints are indicated, but the surfaces are deformed, almost completely destroyed; only traces of old compact bone; some new spongy bone; finely granular calcification in lobularly constructed cartilage; $\frac{3}{4}$ nat. size.

Myxomas of the Bones.—In their pure form, they are very rare (Lucke, Ziegler, Tedenant and others). They originate from the periosteum, or, more frequently, from the marrow (Virchow). The myelogenous myxoma spreads the bone apart, and finally ruptures through as a soft fleshy mass.

The mucoid tissue may become so liquid that cysts result. Usually these myxomas are part of a mixed tumor with chondroma (myxochondromas). Many myxomas are nothing but myxomatous softened chondromas. The combination with sarcoma is also frequent (myxosarcoma). In pure, as well as in mixed tumors, they may produce osteoid and actual bone.

Lipomas of Bones.—They are quite rare, tightly, or loosely fixed to the periosteum, lobulated, and occasionally as heavy as 7 kilograms (lit. Schwartz and Chevrier); the collection at Gottingen contains a preparation consisting of a lobulated lipoma as large as a small fist, coming from the periosteum of the shaft of the femur, and surrounded at its point of insertion by a small bony wall. The author saw a periosteal lipoma on the upper end of the tibia (20 year old woman), and on the femur (38 year old man), in the latter case characterized by many lipoblasts. Intraosseal lipomas are very rare (Wehrsig, lit.).

Hemangiomas and Lymphangiomas.—These are likewise quite rare. In diffuse growth they have been observed in the roof of the skull (the author has a preparation of a hemangioma cavernosa coming from a 76 year old man); they also appear in the sternum, less frequently in the tubular bones, the bones of the face, etc. Gerhardt saw an angioma of the fifth and sixth cervical vertebral bodies, which led to compression of the spinal cord; the author also found such a myelogenous tumor of the sixth thoracic vertebrum which led to a so-called compression myelitis in a 61 year old woman (described by Muthmann). (Lit. Schoene, Saltykow, Ribbert, Fibiger; Trommer, combination of angioma and chondroma.)

Ectatic vessels are quite frequent in various tumors, such as fibromas, myxomas, but more particularly in sarcomas of the bone.

Lymphangiomas belong to the rarest of bone tumors (Wrede, lit.).

Chondromas of the Bones.—Chondromas are cartilaginous new growths. There are differentiated: (*a*) ecchondromas or ecchondroses, which are cartilaginous out-growths of the normal cartilage, and (*b*) enchondromas, cartilaginous tumors in situations of the bones in which normally there is no cartilage, but almost exclusively in such bones which are preformed in cartilage.

(*a*) In the ecchondroses there are differentiated: 1. those which remain permanently cartilaginous (ecchondrosis simplex), as for instance, in the ribs of older people, in the larynx (Putelli, lit.), etc. They are usually small. Later they show a tendency to mucoid or myxomatous softening. Calcification (petrifaction), and ossification frequently occur. 2. Many ecchondroses tend, on the other hand, from the very beginning, to be changed more or less completely into bone (ecchondrosis ossificans or exostosis cartilaginea); for these tumors, see under exostoses, p. 1196.

In the region of the synchondrosis spheno-basilaris, on the clivus Blumenbachii, there occur small, soft, colloid tumors characterized by vesicular cells (physalides), and called ecchondrosis physalifora. Seiffer described one as large as a chestnut. These tumors are believed by some (Virchow), to arise from the cartilage of the synchondrosis, and by H. Muller, Klebs and others (Ribbert and Steiner), to be rests of the chorda dorsalis and therefore are called chordomas. (Histological differentiation of the structure of a fetal chorda and the chordoma by Linck.) According to Ribbert, they take root in the marrow spaces of the bone and spread through the dura. Among other places, chordomas occur also in the sacrum, *i.e.*, in the sacrococcygeal region (Feldmann, lit., Mazzia, Wagner). Mostly small, benign chordomas occasionally become malignant by their mere size (apples, sacral tumor, A. Vecchi), or by actual malignant growth and structure. Grahl, B. Fischer, Linck, Frenkel-Bassal, lit., Jellife and Larkin, lit., Debernardi and others (see lit. by Peters) each described a malignant chordoma. In the case of Peters, metastases were found, also in the case of Potoschnig, who found a tumor in the sacral region as large as a head. [See Eckel, J. L. and Jacobs, W. F., Malignant spheno-occipital chordoma, J. Nerv. & Ment. Dis., 61: 471: 1925.—*Translator.*]

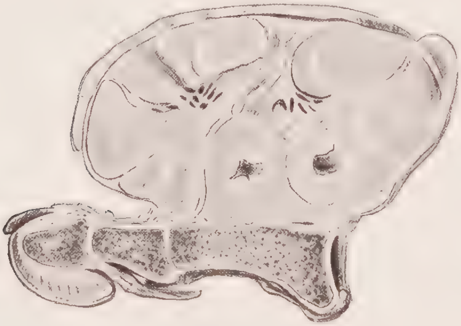


FIG. 623.—Peripheral enchondroma the size of a hen's egg, mobile on first phalanx of second toe; longitudinal sect. through center; 47 year old railroad laborer; 10 years duration; more rapid growth in last 2 years; ¾ nat. size.

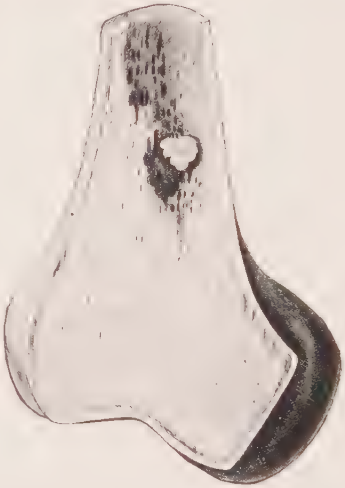


FIG. 624.—Nodular, lobular enchondroma the size of a cherry pit in the medullary cavity of the femur connected with compact bone; man 37, died of septicemia. Alcohol preparation; ½ nat. size.

(*b*) In the enchondromas of bone, there are differentiated: peripheral, and more frequent central growths. Enchondromas also appear not uncommonly in the soft parts, thus, in the parotid (p. 599), in the testes, in the lungs, in the breasts, in the fascias, the skin of the face, the mucosa of the trachea (v. Recklinghausen), etc. Their origin is believed partly metaplastic, and partly embryonal developmental disturbance or aberration, particularly since, in addition to the cartilage, they often contain other tissues. This latter mode of origin has been thought true for the enchondromas of the parotid, the skin of the neck, the thyroid, the mouth cavity, the lips, the breasts, the cartilaginous tumors of the sex organs, chiefly the testes, as well as those appearing in the kidneys. For the conception of testicular chondromas as embryoid tumors (Wilms), see under testes. If many bones are involved, the condition is known as chondromatosis. Unilateral, multiple enchondromas, produced because of disturbances in enchondral ossification allowing cartilaginous masses to persist in the marrow and subperiosteal tissues, particularly in the phalanges, are called Ollier's disease (Bienert). Etiology: many enchondromas are probably of embryonal origin, and arise from persistent cartilaginous fetal rests; others arise from parts of the intermediary cartilage, or follow disturbances in the growth period; it will be remembered that in rickets, islands of cartilage occasionally remain standing entirely separated from the remainder of the cartilage (Virchow, Zeroni, O. Muller and others, see p. 1158); indeed, according to the opinion of these authors, all enchondromas of the bones, internal as well as external, arise from islands of cartilage which belonged to the growth cartilage. In this connection it is interesting to consider the enchondroma illustrated fig. 624 ; it illustrates a forgotten cartilaginous germinal tissue, of course, in the situation, which rarely undergoes development in comparison to the more important cartilaginous tumors. Enchondroma fracturae was discussed on p. 1088. Sites of preference: most enchondromas occur in the diaphyses of the smaller tubular bones, particularly the phalanges and metacarpi, where they are frequently multiple; both hands and feet are involved coincidently with many other bones (Kast, v. Recklinghausen, Steudel, v. Kryger, Nasse, lit.); they prefer youthful individuals (fig. B, p. 1197). But they also occur in the long tubular bones, particularly in the epiphyseal ends of the femur; Schoppig, lit., described a colossal pelvic tumor which necessitated a Caesarian section; on the shoulder blades (point of origin, the edges, lit. Deganello), more rarely the ribs, and vertebrae (x-ray picture by Eug. Fraenkel), they often reach the size of men's heads and larger. Even the upper, and the partly cartilaginous preformed lower jaw (the joint process, Meckel's cartilage and other cartilaginous parts, see Masquelin, Hanau-Koller), are points of origin. Enchondromas do not occur in the membranous preformed bones of the skull. Bones, the site of chondromas, may remain quiescent in their growth and become disproportioned (p. 1198). There is also a familial enchondroma disease (Boyer, Steudel).

The Structure of Enchondromas.- Those of the bones consist, as a rule, of hyalin cartilage (inasmuch as the ground substance fibrillae remain "masked" through the deposit of homogeneous cement substances along the cartilage cells, which does not occur in fibrous and elastic network cartilage, v. Korff); but the ground substance and the capsule often show fibrillae, the former occasionally also elastic fibers. The size and form of the cells and their number vary within wide limits. They produce lobulated, nodular growths of blue white color, covered by vascular perichondrium, and penetrated by vessel-bearing connective tissue septa.

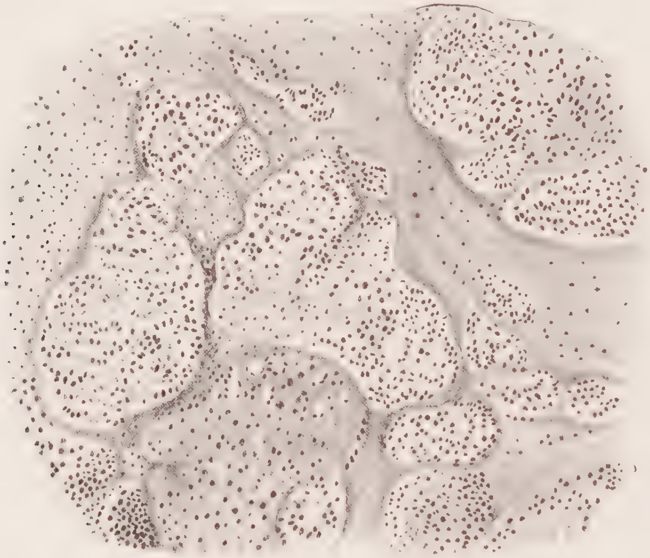


FIG. 625.—Enchondroma, from a pelvic tumor larger than a child's head. Hyalin cartilage, lobulated structure; ground substance of varying density, partly hyalin, partly fluid, partly fibrous; medium magn. (Schoppig, M.f.G. 25, 1903.)

Nutrition is brought from the vascular neighborhood, while the cartilaginous tissue itself remains avascular, or at least, poor in vessels. The tissue of enchondromas (and ecchondromas) shows marked tendency to secondary changes. These are: (*a*) softening by various regressive changes such as fatty degeneration of the cells, vesicular change of the cells (physalides), with simultaneous softening of the interstitial substance, myxomatous change of the ground substance, whereby the cells obtain outrunners (chondroma myxomatodes), total liquefaction of the ground substance with destruction of the cells, which produces softening cysts (see bone cysts, p. 1226). Merkel described the progressive development of myxomatous tissue (and hyalin cartilage), which came from an indifferent germinal tissue (cells and ground substance). Occasionally the softening is manifested by external rupture produced mostly from pressure atrophy, particularly in the multiple chondromas of the fingers which are subcutaneous; there are then produced torpid ulcers and ichorous ulcerating cavities in the tumor. (*b*) On the other hand, chondromas also tend to undergo hardening and calcification (petrifaction), also ossification, by way of the endochondral, as well as the metaplastic routes. Central enchondromas occasionally are surrounded by a shell of bone. But a tumor may consist of bone and cartilage from the very beginning (osteochondroma). (*c*) Transition to malignant tumors has been described (chondro-sarcomas). The cells grow much more rapidly, lose their capsule, become polymorphous (spindle-shaped to giant cell-shaped), lie in heaps, or in nodular lobulated strands close together, and no longer in the cartilaginous ground substance, with tendencies to necrosis; here and there may be osteoid interstitial substance. (For histological details, see K. Mayer; also Deganello.)

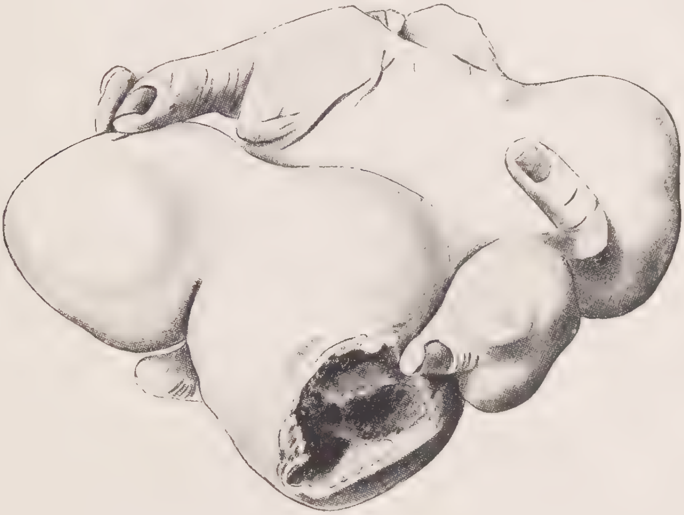


FIG. 626.—Multiple enchondroma of right hand; open, deep, ulcerative cavity in enchondromatous middle finger.

In relation to benignity or malignancy, the enchondromas must be judged with care, since metastases occur in spite of histological benignity, even from pure chondromas. Soft myxomatous forms especially those which tend to grow rapidly after having been present for a number of years, are especially liable to metastasize; thus, for example, enchondromas of the pelvis after softening of the tumor, may rupture into veins and metastases appear in the lungs and liver. French authors emphasize that the exostosis cartilaginea (p. 1197), is particularly a point of origin of such rapidly growing forms of chondromas (lit. Cornil and Coudray). Metastases are usually late in appearance. After extirpation, recurrences are frequent. Extensive formation of enchondromas, chondromatosis of the skeleton, is clinically a malignant disease, in contrast to multiple cartilaginous exostoses (Frangenheim).

Regional metastases and invasion into lymph vessels and lymph nodes is occasionally seen in soft, rapidly growing pure enchondromas. Thus, for example, in chondromas of the scapula, nodular metastases may appear in the neighboring musculature. In mixed chondromas (chondrosarcomas), metastases by way of the blood and lymph streams, as well as recurrences, are much more frequent.

The So-called Osteoid Chondroma (Virchow).—These tumors are not composed of ordinary forms of cartilage, but of osteoid tissue from the very beginning, *i.e.*, they are the so-called cartilaginous bones which stain intensively red with carmine. They often produce collossal masses. An osteoid chondroma resembles a true chondroma only insofar as its consistency is the same and it has a glassy appearance; histologically it has nothing to do with a chondroma. Points of origin: periosteal, from the layers close to the surface of the bone, or central, myelogenous. Osteoid trabeculae with lamellated structure, are arranged in general at right angles to the long axis of the bones; they often anastomose in the network, and frequently break through the external layers of the periosteum as well as the cortex. In these trabeculae there are occasionally embedded rounded cells or cells with prolongations, which, however, have no capsule. Between the trabeculae, the tumor tissue of an osteoid chondroma is fibrocellular, resembling marrow, and containing osteoblasts; it also contains numerous capillaries, an important differentiation between the avascular tumor tissue of enchondromas. Sites preferred are the long tubular bones, chiefly the lower end of the femur, the upper end of the tibia, the humerus in younger individuals, occasionally in the skull. In its growth, the tumor takes on a spindle, a pear, or a club shape, inasmuch as it grows more and more toward the diaphysis. The surface of the tumor is relatively smooth; on section, even of very large tumors, the contours of the old bony cortex are usually indicated here and there; the bone traverses the middle of the tumor, is partly destroyed or sclerosed. The purely osteoid parts appear like fibrous cartilage on section, but are hyalin and transparent here and there, while in other situations they are vesicular, lamellated, or reticular. The consistency of the osteoid is soft, elastic, cuttable, like fibrous cartilage or like callus. The lobulated structure of enchondromas is lacking in osteoid chondromas. The size of osteoid chondromas may become quite enormous. v. Volkmann describes a specimen from the femur, which reached a diameter of 66.7 centimeters.

Whereas the osteoid chondroma shows no tendency to softening in contrast to an ordinary chondroma, it, on the other hand, shows a marked tendency to take up calcium, and to produce true bone. But calcification frequently occurs merely in some of the trabeculae, and the tumor is readily cut with a knife, or the deposit is quite irregular and thick, so that insular or coral-like petrifactions and not true ossification occur; in other cases, particularly the centers and bases become changed into porous or dense bony tissue, while the peripheral younger layers remain free; in other cases, the ossification is universal, and the osteoid chondroma (osteoidoma) becomes a hard osteoma.

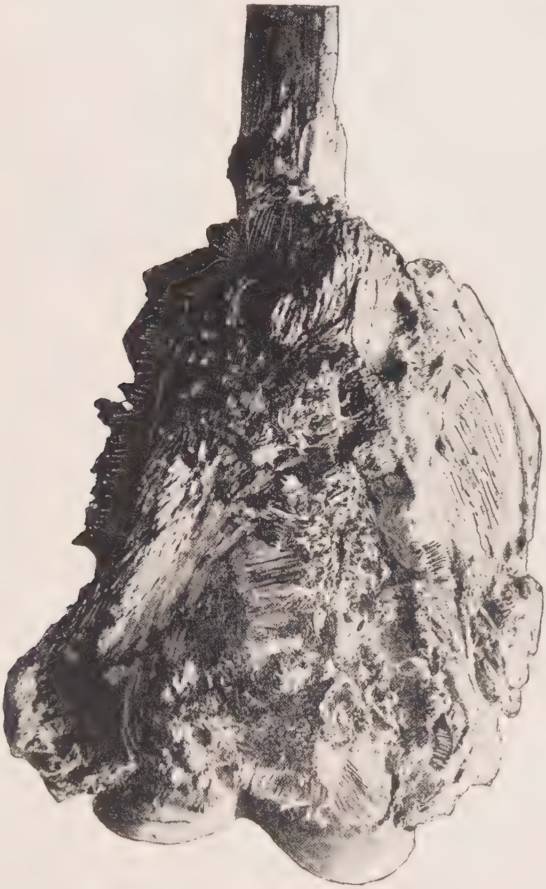


FIG. 627.—Skeleton of an osteoid sarcoma the size of a child's head, of lower end of femur, from unmarried woman of 43.

This histologically benign tumor is clinically to be looked upon with suspicion like the ordinary enchondroma. The tumor may rupture into veins and produce metastases. Transitions to enchondromas as well as to sarcomas have been recognized.

The osteoid sarcoma is the richly cellular, malignant variety of an osteoid chondroma. Most of the tumor tissue becomes sarcomatous and contains a homogeneous matrix of soft osteoid tissue which becomes ossified to more or less extent by taking up calcium. Occasionally it is merely calcified (petrification), instead of changed into bone (Dietrich, Buerger). The osteoid may produce anastomosing trabeculae and delicate networks as in a spongiosa, while the marrow tissue is invaded by sarcomatous structure. The point of origin is similar to that of osteoid chondromas.

In macerated preparations, the ossifying, calcified, fragile skeleton of the tumor is characterized by great irregularities—a mass of spongy, tough, spinous, crooked, ossifying and calcifying material (fig. 627).

Sarcomas of the Bones.—Sarcomas are the most frequent and the most malignant of bone tumors; they are of great practical importance (Anschutz). Some are soft, some are hard; the hardest ones are bone-producing osteosarcomas. An osteosarcoma is not simply a sarcoma of the bone, but a sarcoma producing bone tissue. It need not necessarily arise from a bone. There are differentiated two chief groups of bone sarcomas: (*a*) the very malignant peripheral or periosteal, and (*b*) in general, the less malignant, in part, relatively benign, central, myelogenous or endosteal sarcomas beginning in the spongiosa or in the marrow cavities. This division is not always easy to use, and it is often difficult to determine the exact point of origin (see Ribbert, Rumpel and Buerger's new classification).

(*a*) **Periosteal, Peripheral Sarcomas of the Bones.**—These are located chiefly in the ends of the long tubular bones, but occasionally arise in other situations of the skeleton. There may be differentiated softer and harder forms. The soft, bacony are, however, usually fairly firm, particularly in comparison to a number of fleshy, soft, or almost fluid myelogenous sarcomas. Histologically, they are composed of round cells, spindle cells, mixed cells, or polymorphous large cells. Periosteal sarcomas occasionally show an alveolar arrangement (p. 1209). Giant cell sarcomas also occur (fig. 249 on p. 573). Round cell sarcomas are more malignant than spindle cell sarcomas; among the latter, the small cell types are particularly vascular and more malignant than the large cell forms which frequently show transitions to fibromas. Chondrosarcomas are also met. Sarcomas may gradually surround a bone, and in younger individuals produce enormous tumors in a relatively short time (circumference of one leg is one meter or more). Occasionally they take on a spindle, or pear-shaped contour. In the beginning, the tumor masses can still be differentiated from the compact substance of the bone, and may be bounded externally by the periosteum. The structure is fibrous or more homogeneous, and not rarely shows radiating, bundle-like structures. The latter is especially the case, when the tumor shows more or less tendency to produce osteoid or completed bone tissue (osteosarcoma or osteoid sarcoma or ossifying sarcoma). Here the tumor tissue itself, sometimes in small degrees, sometimes over extensive areas, is changed to osteoid or to bone. This usually attaches it to a bone, from which radiate coarser, or finer, occasionally tubular, bony trabeculae and needles. In macerated preparations, formed rays and bundles separate toward the periphery (figs. 609 and 630); in other cases there are ivory hard or porous exostosis-like nodules (fig. 611). The bony trabeculae are often but loosely connected, so that macerated preparations are extremely fragile. During maceration, a part of the tumor skeleton is lost, since many parts remain free in the soft tissues. More rarely a shell is formed, which usually shows holes in large, rapidly growing tumors (fig. 610). The soft tissue of many sarcomas shows a marked tendency to undergo regressive changes, such as fatty degeneration, necrosis, hemorrhages, which occasionally leads to rupture through the skin. The section surface is variegated.

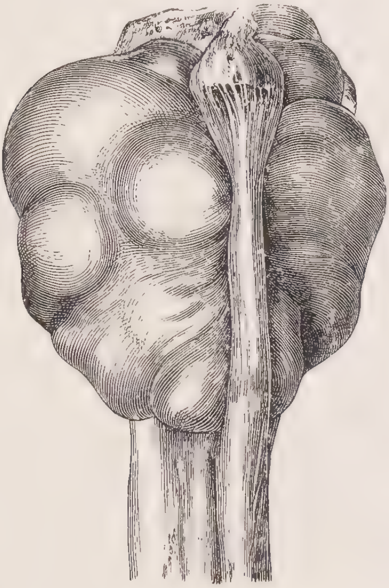


FIG. 628.—Periosteal sarcoma of tibia from a boy. (From Billroth Allg. Chir.)

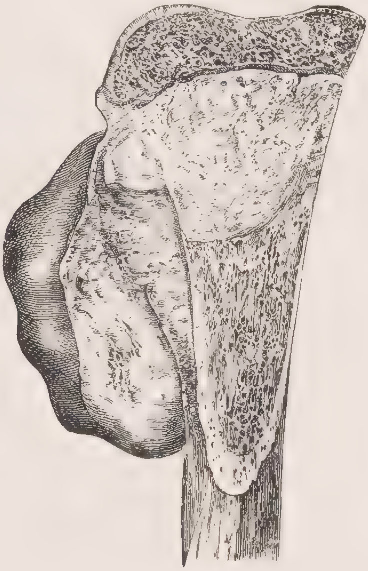


FIG. 629.—Cross section of fig. 628.

The further growth of a periosteal sarcoma may so occur that the tumor masses rupture into the soft parts of the neighborhood. (According to Marullaz, the periosteum at the border of the tumor participates in the tumor growth by undergoing sarcomatous change; this is opposed to the view of Ribbert, who believes that periosteal sarcomas come from the spongiosa of the diaphysis, and can spread only subperiosteally.) The bony parts bordering on the tumor, or surrounding it, may be traversed and rarefied by invading tumor masses (fig. 629), so that spontaneous fractures result, or the bone undergoes the hardest kind of sclerosis by way of an ossifying ostitis or osteomyelitis. As ossifying sarcomas spread, many partly ossified tumor nodules appear in the surrounding soft parts. Even the metastases, particularly those in the lungs, but also those in lymph nodes, or in far distant parts, for example, the brain or the roof of the skull, may ossify or partially calcify—or remain entirely soft. In the lungs, innumerable nodules may appear, some as large as fists (as in fig. 217, p. 479). Gigantic metastases also occur, occasionally in the pleura (p. 494).

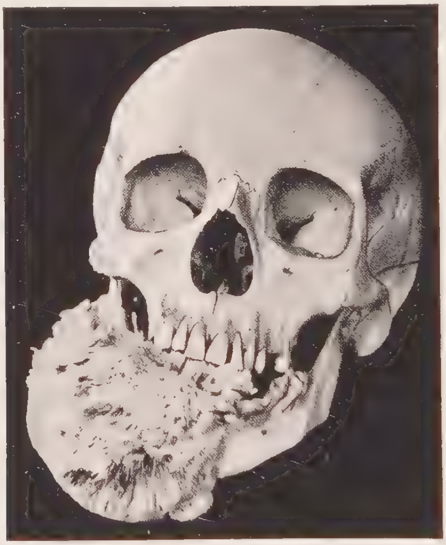


FIG. 630.—Ossifying periosteal sarcoma (so-called osteosarcoma) of lower jaw with formation of radiating bundles of finest fragile bone spicules; 1/3 nat. size.

(*b*) **Myelogenous, Central Sarcomas of the Bones.**—The histologic structure of the central sarcomas of the bones is variable. Among others, there occur: small or large cell, soft, richly vascular, round cell sarcomas, fibrocellular, or pure spindle cell sarcomas, which likewise may show cells of different sizes. Embedded giant cells are frequent in the fibrocellular, or pure spindle-cell masses, often quite astonishing as to number and size. This is the ordinary giant cell sarcoma. Others show strikingly large, polymorphous, sometimes multinuclear cells, occasionally pointed cells with large pale nuclei. The cells are grouped into strands and heaps, and often lie close to each other so that they resemble carcinoma. These are called alveolar sarcomas, a name also applied to similarly constructed sarcomas of the periosteum. The reticulum may be very tender, composed of spindle shaped cells, of isolated fibers, or of outrunners of the sarcoma cells. The cell masses, often epithelial-like and pressed closely together, are in intimate contact with the alveolar walls; if attempts are made to remove them from the alveoli, in contrast to carcinoma, it can not be done easily; the spaces are not quite empty (as in carcinoma), but very fine fibrils usually remain coursing through the alveoli (reticulum staining!); see fig. 631.

Many myelogenous sarcomas are particularly rich in telangiectatic capillary vessels (telangiectatic sarcomas). Others are hemangiosarcomas; among these are a number of varieties. Many produce thick collars or tubes of rounded or angular, thickly placed cells around capillary blood vessels, as in fig. 632 (perivascular sarcoma or tubular angiosarcomas; for illustrations of this form of sarcoma, see under dura mater, where generalizations are stated concerning sarcomas; see also p. 179). In other tumors, fat containing, cells (fig. 633) are placed radially around capillary vessels (so-called perithelsarcoma or peritheliomas; lit. by Bevacqua). Where neighboring collars coalesce, or where the cell growth is particularly diffuse, the impression is given of a diffuse sarcoma and the angiosarcomatous character is completely lost. Others are hemangioendotheliomas with delicate, cubical, epithelial-like cells resembling adenomas, adenocarcinomas, (Cottis) or alveolar sarcomas (Martens,

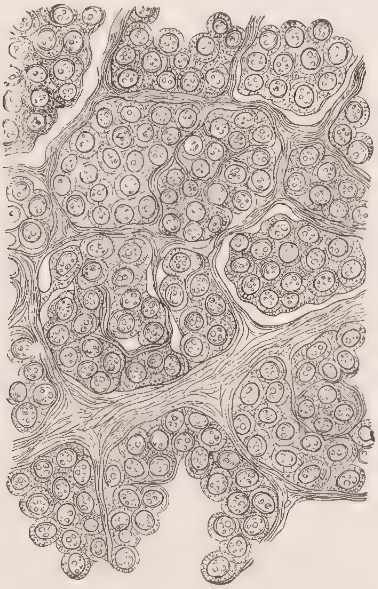


FIG. 631.—Alveolar sarcoma from the tibia. (Billroth's Allg. Chir. 16th Edit.)

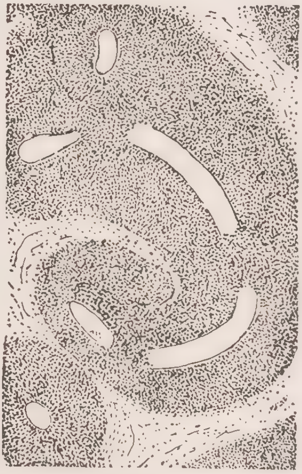


FIG. 632.—Perivascular sarcoma (hemangiosarcoma) of bone marrow. Blood vessels surrounded by an intensively stained thick layer of sarcoma tissue. (Low power.)

Schlagenhaufer), but their alveoli are filled with blood; they may also be mistaken for the metastases of other tumors such as carcinomas and particularly, hypernephromas (Rost, lit.). These tumors prefer the upper diaphyseal end of the humerus (lit. by Zetkin, Avenarius). Occasionally the tumor tissue produces delicate anastomosing osteoid or true bony trabeculae, or thicker, often unshapely, bony trabeculae (see under osteoid or osteosarcoma). Similar tumors have recently been described as osteoblastomas on the ground that they deserve a separate position under

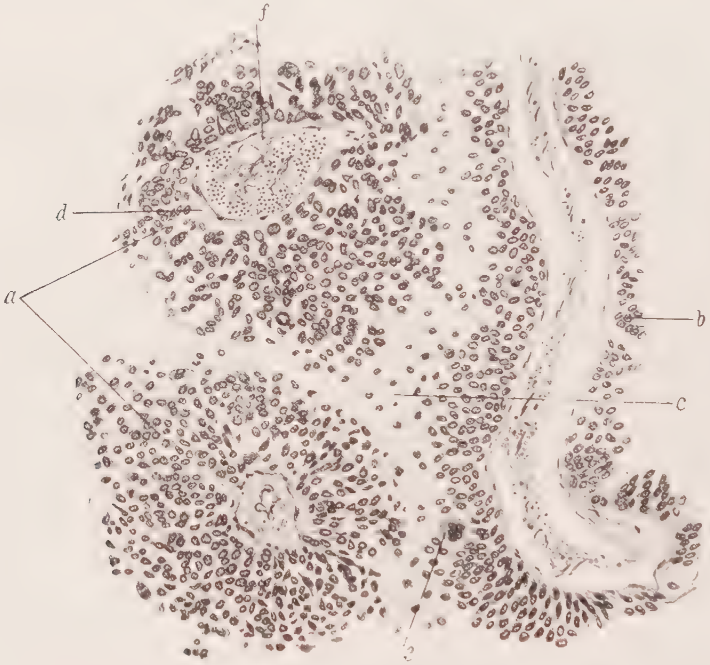


FIG. 633.—Perivascular hemangiosarcoma (so-called perithelioma of bone marrow, after Bevacqua, l.c. 947). a, cross section; b, longitudinal section through central blood vessel (containing blood corpuscles) and f, fibrin with cell cloaks; c, empty spaces (artefacts). (Medium magn.)

sarcomas of the bones; these contain systems of osteoid or ossifying trabeculae, between which, in a network of stroma, are masses of epithelial-like, closely applied, osteoblasts, which cover the trabeculae like an epithelial cover, whereby minute papillary pictures are produced (Herxheimer, v. Hansemann, Herrenschmidt). Lubarsch speaks of these as "adenoma osteoblastosum." Buerger and others speak of osteoblastosarcomas, and understand by this term, tumors, composed of solid alveoli of osteoblast-like cells with many scattered giant cells, with the ability to produce bone, which is also seen in the metastases. They are easily mistaken for hemangioendotheliomas, and their malignant varieties (p. 179), or for metastases, particularly when nothing is presented for examination except an isolated bone.

As stated on p. 1193, a new bony shell is often formed during the further growth of the tumor, particularly if a giant cell sarcoma; this is produced from the old bony substance externally from the periosteum (fig. 607 and 634). If the shell is quite thin it may crepitate on pressure like parchment.

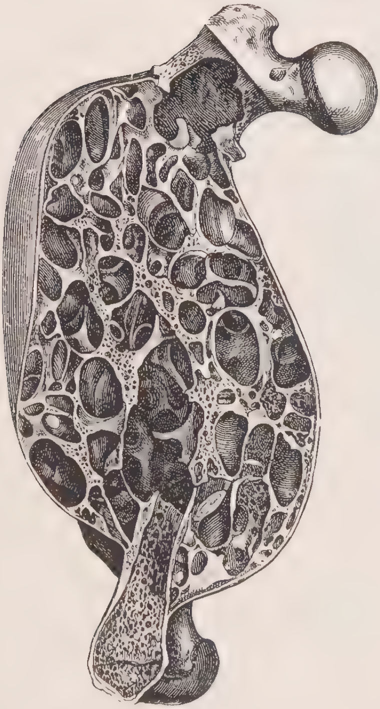


FIG. 634.—Large cystosarcoma; cystic shell or capsule sarcoma of upper thigh derived from myelogenous giant cell sarcoma. Many bone trabeculae in the walls between the cysts (after Pean, from Billroth's Allg. Chir.).

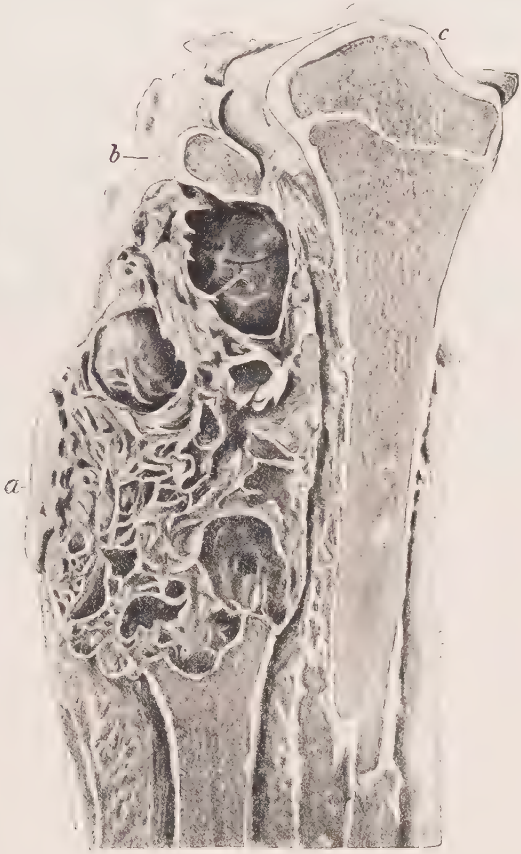


FIG. 635.—Polycystoid giant cell sarcoma of upper metaphysis of fibula; a, perforation through skin; b, epiphysis; c, tibia; frontal section; ½ nat. size.

Other, very soft, myelogenous sarcomas are not surrounded by a shell or show merely attempts at this formation. These are less common. The type as illustrated in fig. 636 is relatively frequent. Occasionally the section surface shows a radial or fascicular structure; the bundles consist chiefly of spindle cells. In other cases, the section surface is homogeneous (round cell tumors), or brittle and variegated (giant cell sarcomas, fig. 636).

Spontaneous fractures readily occur when the tumor masses invade the cortex from the marrow, whereas, in other cases, the central tumor grows through the cortex without much destruction, and then spreads on the free surface (p. 1193).

Regressive changes are frequent in the tumor masses and consist of: myxomatous softening, liquefaction and cyst formation, fatty changes, necrosis, hemorrhages, the latter leading to pigmentation and also to cyst formation. (Details by Ribbert.) Occasionally, a very large part of the tumor tissue is destroyed and liquefied, often to merely a thin coating along the edges (cystosarcomas, fig. 636). The microscopic diagnosis of small biopsy specimens is exceedingly difficult!

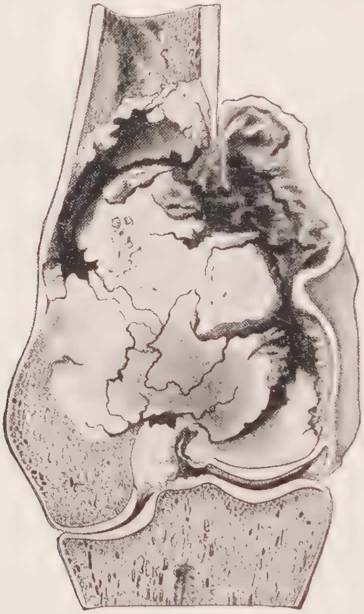


Fig. 636.—Myelogenous giant cell sarcoma of lower epiphysis of femur with extensive necrosis, crumbling; blood saturation and softening of tumor masses; esp. destruction of external condyle; no formation of bone shell; young woman; after a fall 8 months before; after spontaneous fracture assumed valgus position; some fever; ½ nat. size.

Rich vascularity and hemorrhages in cystic myelogenous sarcomas occasionally produce pulsation and systolic blowing or rubbing noises which may be mistaken for the signs of bone aneurysm. Among others, the author saw this occur in a shell sarcoma of the upper end of the ulna which had been mistaken for a bone aneurysm; the tumor grew five months after trauma and it was only by microscopic examination of the curretted soft wall that the condition was recognized as a spindle cell sarcoma rich in giant cells. The actual occurrence of bone aneurysm is doubted by many (Nakayama).

The sites of election of myelogenous central sarcomas are chiefly the jaw, particularly the lower jaw. Many of those tumors called epuli, (p. 573), are histologically central giant cell sarcomas; others are periosteal giant cell sarcomas. (Consult "brown tumors" under ostitis fibrosa, p. 1111.) Other sites are the epiphyses, *i.e.*, the ends of the long tubular bones (lower end of the femur—fig. 636—upper end of the tibia), rarely as in fig. 608, the diaphysis, the ends of the radius (fig. 607) and the ulna. More rarely, giant cell sarcomas have been observed in the lumbar vertebrae (Madelung, lit. and Schumann, R. Lehmann), or in other smaller spongy bones, as for example, the talus (Dietrich in the calcaneus, see Valentin, lit.). Central sarcomas of the sternum (Buschmann, lit.) and of the clavicles and other bones, are rare.

The Course and Prognosis of Bone Sarcomas.—Giant cell sarcomas of the bone (central bone sarcomas in general) are usually solitary, and some are relatively benign, *i.e.*, show little tendency to general spread; indeed, on consideration of the "brown tumors" of giant cell sarcoma structure, which we meet in ostitis fibrosa (p. 1111), and which are regarded as chronic inflammatory, reactive, or resorptive processes, the tendency is often to regard giant cell sarcomas of the bone, in general, as relatively benign, purely local tumors, and not as true malignant sarcomas. This is quite true of the myelogenous epulides which are rich in giant cells (see above, and p. 573), which appear chiefly at the time of second dentition; it is true that they recur locally, when they are not removed with a part of the alveolar process, but metastases are not produced, and some sort of relationship to ostitis fibrosa is very probable. The giant cell sarcomas of the long tubular bones must, in relation to their course, be regarded, at least in part, as malignant (Anschutz), because, even though not regularly, but often enough, they invade surrounding soft parts (as the author saw in a 17 year old girl with a giant cell sarcoma of the lower metaphysis of the femur, invading the musculature), and further because of the appearance of distant metastases, particularly in the lungs. Occasionally gross invasion of tumor masses into the veins may be demonstrated. The giant cell sarcomas are, however, always the most benign of the sarcomas. Ribbert, who believes giant cell sarcomas are a part of the bone resorbing tissue, in contrast to the osteosarcomas, which come from bone building cells, explains this mild malignity of the former, by assuming it has diminished growth energy. If an extremity is amputated because of sarcoma, the veins must be carefully examined in the amputated member, in order to gain some information for the prognosis.

Among the periosteal sarcomas, those that are softest and most richly cellular are the most malignant. Concerning the tendency to metastasis, which in these is much more frequent than in the myelogenous varieties, particularly to the lungs and the lymph nodes, the conditions in isolated cases vary considerably. In general, it may be said that a sarcoma is the more malignant, the smaller its cells.

In the etiology of sarcomas of the bone, traumata probably sometimes play an essential role, even though spontaneous origin from unknown grounds without trauma, usually in otherwise healthy individuals (15 to 30 years of life), is certainly the rule; unquestionably, trauma may increase the rate of growth of a tumor; it is also possible that trauma may release a previously present tumor, or allow a tumor to grow in one who has had a predisposition to a new growth. Important points of view in this matter are: a sufficiently serious injury; application of the trauma to the site where the tumor is manifested; corresponding time between the trauma and the manifestation of the tumor—this need not always be short, but with Eug. Fraenkel, it can be admitted that a long time may elapse between the two events; the histological character of the tumor must also correspond, (see Pick; also Anschutz). Platau believes quite correctly that a traumatic origin of bone cysts is possible in younger individuals, as well as a new tissue growth similar to giant cell sarcoma (also shown by Fujii); the course is, however, benign. The development of sarcoma has certainly been observed in situations of fracture (the same is true of osteoid chondromas, see the case of Konjetzny); it is necessary, however, to be quite careful in judging, since primary myelogenous, as well as metastatic tumors, frequently lead to secondary spontaneous fractures. The collection at Breslau contains a preparation from an old woman, in whom, after resection of the knee joint because of fungus (synovial form, microscopically diagnosed), a polymorphocellular sarcoma developed 8 months later in the well ossified consolidated place of union, which, as a hen's egg size growth, protruded from the situation of the resection. (See also Pfeiffer, lit.) Klemm saw a round cell sarcoma after an osteomyelitis. In general, most bone sarcomas are found between the ages of 11 and 20, *i.e.*, in puberty. Congenital bone sarcomas are very rare; Goebel (lit.) described a spindle cell sarcoma in the femur of a 3 weeks old boy.

Rarer, Particular Forms of Richly Cellular Bone Tumors.—Primary multiple myelogenous tumors of the bone marrow under the general name of myeloma (lit. in appendix), sometimes occur with swelling, often, however, without any, or merely mild changes of the external configuration of the bones; they originate internally, particularly in the vertebrae, the sternum, the ribs, bones of the skull, more rarely in the long tubular bones as in the femur, but occasionally in almost all the bones. They are sharply circumscribed, occasionally as large as hen's eggs, soft, according to their vascularity, pale, gray red or dark red, well differentiated from the marrow, which is substituted by rounded nodules or ragged shreds; some appear in the compact bony tissue, which they destroy with perhaps spontaneous fractures. Particularly in the roof of the skull (fig. 637), numerous furrowed and perforated defects result from maceration, as observed occasionally in metastatic tumors. The condition occurs with degeneration of the marrow (Bender), always with high degrees of destruction in the skeleton, and outspoken clinical symptoms from the bony system, among others, early spontaneous pain and great tenderness on pressure, swelling around the tumor, perhaps multiple spontaneous fractures which heal rapidly and very easily, deformities of the vertebral column, perhaps with spinal cord symptoms, and shortening of the trunk. With the symptoms of progressive weakness, anemia and cachexia, the disease practically always ends fatally in months to years. Older men are affected more often than women. The question of metastases is much argued; it is closely related to the question of whether the myelomas are hyperplasias or true tumors, whether the latter may appear from the former, and whether these tumors are benign or malignant. Nodular myeloma formation occasionally occurs in other organs, such as the spleen, liver, kidneys, lymph nodes and others, and produces the picture of metastatic nodules. It is, however, probable, that these are not true metastases such as occur in malignant tumors, but merely an expression of a systemic disease of the hematopoietic apparatus, so that we look upon these myelomas in the same manner as Pappenheim, Lubarsch, H. Hirschfeld (lit.), v. Domarus, Eug. Fraenkel, and others. While this system disease is confined, as a rule, to the bone marrow, there occasionally appear structures similar to the foci in the bone marrow in the same organs which are invaded by foci in hyperplastic leukemia and pseudoleukemia; in the latter disease, however, most authors assume the foci are of autochthonous origin, a myeloid metaplasia, but a few still believe in cellular transportation and further growth. Because of the undoubted resemblance to these processes, many now believe that myeloma is a form of aleukemia (pseudoleukemia), with medullary localization in the majority of cases (Hart, Eug. Fraenkel and others), and therefore disagree with the idea of the true tumor nature of myelomas. In addition to macroscopic nodules in the organs, occasional microscopic myelocytes are found in the blood from the spleen, the liver and other organs (Saltykow, and others); in the lymph nodes are whole colonies of these cells (Sternberg, Mieremet); Glaus speaks directly of tumor tissue (myelocytes) in the lymph nodes, while Lunghetti, who is of the opinion that a purely hyperplastic myeloma may later become, or take on more or less neoplastic character, attempts to differentiate between myeloid transformation in the sinuses, and myelomatous intravascular nodule formation in the stroma of the lymph nodes which he believes is true metastasis. Those cases showing typical myeloma structure, but organ metastases, are called myelosarcomas by Harbitz, and the case of Hoffmann, a plasmacytoma, because of "liver metastases," *i.e.*, a malignant tumor. Sternberg and Menne believe the case of Hoffmann should be separated from true myelomas because of the liver metastases. If the condition is regarded from the point of view of a systemic disease, the opinions of Harbitz and Hoffmann will not be adopted, but neither can the doubts of Sternberg and Menne be recognized.

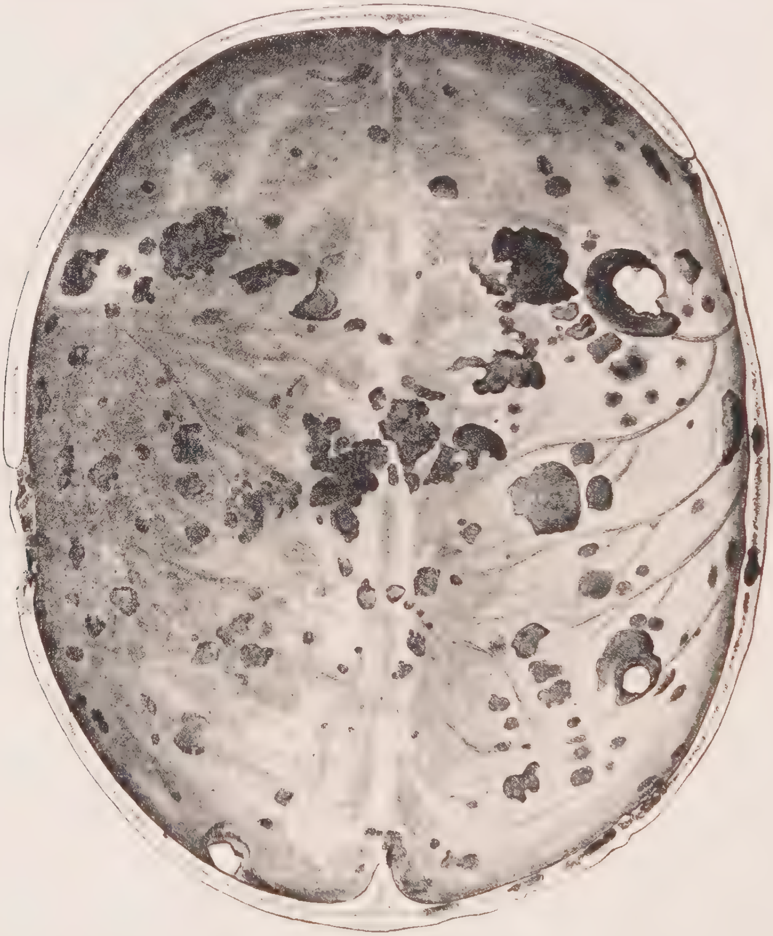


Fig. 637.—Multiple myelomas of roof of skull of man 42 years old; also had tumors in spinal column, ribs, sternum. The brown red myeloma tissue was of soft consistency, easily cut. Preserved in Pick's sol.; ⅔ nat. size.

Histologically, these tumors, because they arise in the marrow may well be grouped under the term "myeloma" (lit. Hirschfeld, Herz, Wallgren and in the appendix), and may be divided into a number of groups:

(*a*) Typical myelomas (myelocytomas and myeloblastomas), are primary multiple tumors of the bone marrow (v. Rustizky), which are recognizable by an enormous hyperplasia of the marrow, chiefly, even though not exclusively, of the red marrow, particularly that of the trunk skeleton, in which a remarkable uniformity of cells, resembling myelocytes, *i.e.*, the characteristic elements of the bone marrow, dominates the picture (myelocytoma). These are larger, or smaller, rounded, or angular cells from appositional pressure, with neutrophilic granules, lacking in some cases, (called myeloblasts, the non-granular predecessors of the myelocytes; see Herxheimer, Menne, Permin, lit., Hart, Dialti, lit., Berblinger). The color of these tumors is dark red from rich vascularization, or hemorrhage; not rarely their centers are necrotic. They appear in all parts of the skeleton in which red marrow is found either as nodules or diffusely spread. When the growth is diffuse, *i.e.*, without the formation of outlined nodules, the name myelomatosis is used.

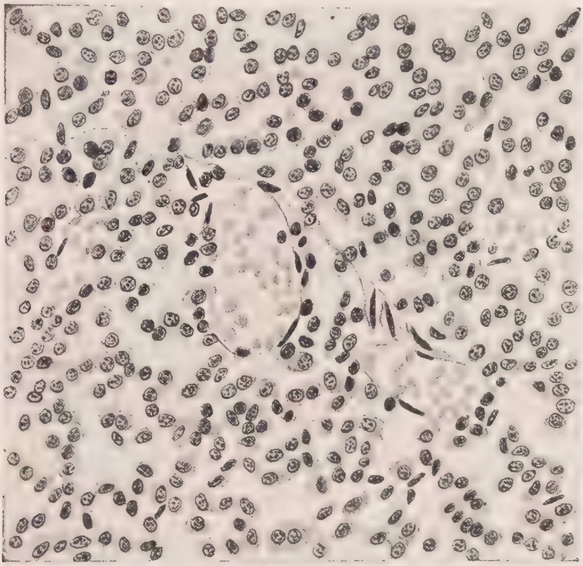


FIG. 638.—Myeloma (myelocytoma) from second lumbar vertebra of woman of 43. (Med. magn.)

(*b*) As an erythroblastoma, Ribbert described a case in which the cells, according to his opinion, contained some hemoglobin, but it was later shown that degenerated myeloma cells sometimes contain substances in their protoplasm which stain like erythrocytes (lit. by Wallgren). Schridde described an erythro-myeloblastoma, Froboese, an erythroblastoma mixtocellulare (with calcium metastases).

(*c*) Still other cases have cells of the character of the large "mononuclear" leucocytes of the blood (MacCallum). These are called leucocytomas.

(*d*) Other cases show cells of the character of plasma cells (case of Hoffmann, combined with myelocytes, cases of Aschoff, six cases of Christian, lit., case of Berblinger, Simmonds, Verse, Warstatt, Kimmerle-E. Fraenkel and others); but Sternberg and Menne (lit.) do not believe that the case of Hoffmann is a true myeloma since there were metastases in the liver; Mieremet, probably correctly, believes that the absence, or presence of "metastases" (see p. 1217), is not a strict differential point. The names plasmacystoma, plasmoma, plasmacellular myeloma, are used to describe these peculiar subtypes of a lymphoid form of myelomas (Verse), while others (Sternberg) speak of granulomas in contrast to hyperplastic true myelomas. Lately, Klemperer (Institute of Sternberg), agrees with Verse's conception. Plasma cells may also appear in the circulating blood. According to Neckarsulmer, most of the multiple myelomas are of this type (see Simmonds), but this is doubted by the author.

(*e*) The tumor tissue shows a structure somewhat similar to lymphadenoid tissue, but in rare cases is also rich in polymorphonuclear giant cells. Many call these tumors lymphocytomas, or the lymphocytic form of myelomas; these tumors do not, however, consist only of lymphocytes, but of rather atypical lymphoid tissue, such as in lymphosarcomas, for which reason the author, with Wieland, on the basis of five of his own observations, prefers the latter designation, and also because this tumor may show heterotopic growth and metastases. But too great weight should not be laid upon the last factor since similar pictures are seen occasionally in typical myelomas (p. 1216), which are not true malignant tumors; it is thus better to speak of aleukemic lymphomas or "pseudoleukemic" tumors than lymphocytomas, because, as has been pointed out, these are obviously not true malignant tumors, but a system disease of the lymphatic-hematopoietic apparatus. Points of origin may be specific cells of the marrow, but this has not been shown beyond criticism; perhaps it is necessary to think of lymph nodules (p. 287). The color of these tumors is often pale gray to white. In contrast to the myelomas, they appear (*a*) in the long tubular bones, and not only in the red marrow; they produce, even though rarely, metastases in the internal organs; occasionally they invade the neighboring parts, such as the periosteum, pleura, and muscles. In addition to predominant bone resorption, there are occasionally indications of new bone formation. Cases with extensive sclerosis (Hammer), probably do not belong in this category.

Berblinger would use the name myeloma only for those structures composed of parenchymatous bone marrow cells, as (*a*), (*b*) and (*c*), which are formed in the bone marrow itself. But Wallgren (lit.), in his critical work, came to the conclusion that all of the various cell forms in the different cases of myeloma cannot be sharply differentiated, but—which Shennan also believes—are possibly merely various forms or different degrees of differentiation or development of the same cells, and that it is best to gather them together under the uniform name of "myeloma cells," and not to speak of myelocytes, myeloblasts, lymphocytes, etc. By this means, of course, many difficulties of classification, and probably also many errors of judgment, will be removed. Lit. concerning myelomas by Isaac.

In the myelomas there may be a particular reaction in the urine, (precipitation at 55°, increase of the cloudiness at 65°, and from here gradual dissolving until 85°; reprecipitation on cooling, a characteristic pathological albuminous body, Bence Jones' bodies; Kahler). According to Schutz (lit.), however, this is lacking in about half of the cases. (Concerning nephrotic changes, see lit. by Thannhauser and Krauss.) But this reaction may occur in lymphatic leukemia, among other conditions (Askanazy, and lit. by v. Domarus, Hirschfeld, Herz).

See lit. by Glaus, concerning amyloidosis in myelomas and amyloid of a peculiar structure in myelomas; see Block, concerning a peculiar dermatosis occurring with elastolysis in Bence Jones' albuminuria. See also below.

The multiple intravascular endotheliomas of the bone marrow (Marckwald), are a particular group, possibly identical with the multiple bone peritheliomas of Bignami, and Bevacqua.

Marchand observed a general sarcomatosis of almost the entire skeleton with non-characteristic round cells (somewhat like marrow cells), following a primary myelogenous sarcoma of the skull. A case similar in many respects with a sarcoma nodule in the left adrenal, is believed by M. B. Schmidt to be a pseudoleukemic disease; possibly the case of Marchand, and those of Gussenbauer-Chiari and Dittrich, are similar. All occurred in youthful individuals, and were roughly similar macroscopically. Allied to these cases are two described by Roman (lit.) as myeloplastic sarcoma; primary multiple malignant tumors of the bone marrow, with metastases in the lymph nodes and the liver, were regarded by Roman as a systemic disease of the myeloid tissue of the skeleton; the tissue was composed in large part of undifferentiated cells of the myeloid system; particularly striking was the nodular thickening of the roof of the skull (see illustrations by Roman).

Concerning the chloromas, which are colored multiple periosteal new growths, see p. 272.

In a case of Hedren, a very rare amyloid tumor (p. 323) of the bone marrow of a rib as large as a fist was mistaken clinically for a sarcoma;

see also the cases of Edens (amyloid tumors of the sixth rib) and Schmid, (lit.), (hen's egg size amyloid tumor of the upper jaw, amyloid fibrosarcoma, occurring together with epidural and prevertebral amyloid tumors). [For clinical etc. see Coley W. B. and Coley B. L., Arch. Surg. 13: 779: 1926 and 14: 63: 1927.—*Translator.*]

Secondary Tumors of the Bones.—Among the secondary tumors, the chief forms are carcinomas and sarcomas. Among the latter, the melanotic sarcomas often produce innumerable metastases in many, sometimes in all, of the bones. In very rare cases, an ordinary bone sarcoma metastasizes almost exclusively in the skeleton; see the case of Nunokawa.

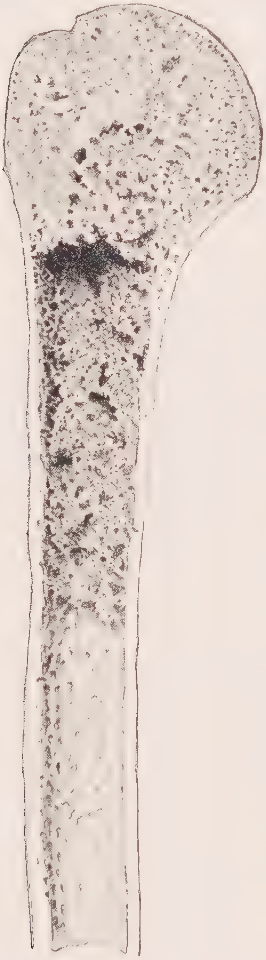


FIG. 639.

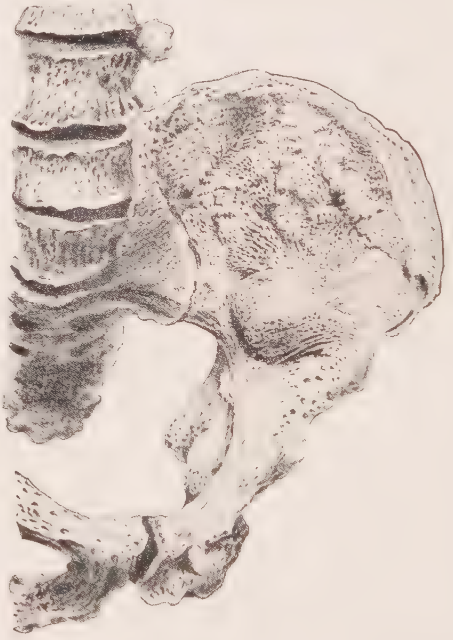


FIG. 640.

FIG. 639.—Osteoplastic carcinoma (spongioid) of r. humerus from carcinoma of prostate; man 67 years old; ¾ nat. size; (see Kaufmann, Malig. Tum. des Prostata, Deutsch. Chir., No. 53, 1902).

FIG. 640.—Osteoplastic carcinoma of l. half of pelvis from carcinoma of prostate; man 72 years old; ¼ nat. size; (see ref. above).

Carcinomas do not occur as primary growths in the bone, but occasionally an old bone fistula lined by skin from the epidermis, gives rise to a carcinoma which may grow into the bone, and resemble a primary bone tumor. By direct extension of a carcinoma, particularly of the skin, (see Nakahara), is produced a carcinomatous caries, which leads to fracture (fig. 96 , p. 169). Although secondary or metastatic carcinomas of the bone brought there by way of the blood stream, prefer not only certain bones, but, in these, certain situations which v. Recklinghausen believes is due to static factors, those situations are preferred in general, on which permanent pressure and pull is exerted most intensively. The situation of first obstruction met by the carcinoma cells coming in the blood through the vasa nutritia, are the smallest, but relatively broad, veins of the bone marrow. Foci in the marrow or in the spongiosa may later grow into the periosteum through the corticalis inside of the vessel paths. The histological character of the metastasis resembles more or less that of the primary tumor.

According to their form, the metastatic carcinomas are circumscribed, nodular, diffusely infiltrating, partly destructive and osteoclastic, producing caries of the bone, which is the most frequent form, or osteoplastic, whereby a fine spongioid (fig. 639) or an ivory-hard condensed bony tissue arises (fig. 641), which may lie upon the bone like a tumor (fig. 640). In extensive diffuse tumor infiltration occuring at the cost of the old bony tissue, the bones may become spontaneously painful, and be tender on pressure, occasionally also elastic, and show infractions (carcinomatous osteomalacia). The blood picture (p. 193), may correspond to that of a severe anemia. It is the infiltrating type which is particularly prone to produce rich, partly osteoid, partly calcified, new bone tissue, which progresses hand in hand with the increase in number of the specific carcinoma cells and with the resorption of the old bony trabeculae (osteocarcinosis, v. Recklinghausen). It is, however, questionable whether this osteoplastic process is due to stasis from obstruction of the efferent bone veins, or to irritating chemical substances coming from the carcinoma; these factors are important in the formation of the callus in spontaneous fractures, which occurs in spite of the presence of carcinoma (Troell); see Assmann, who believes that the new bone formation is related to small bone necroses which irritate or stimulate. Microscopic pictures are met in which the alveolar framework of the carcinoma or the carcinoma stroma, has been changed into osteoid, or into bony trabeculae newly formed. The interalveolar connective tissue which belongs to the fibrous marrow produces new bone partly through neoplastic processes and partly through metaplasia. New bony substance may also be deposited upon older trabeculae. In situations where there is little new bone produced, but in which the older bone trabeculae are absorbed, the thickened fibrous carcinomatous marrow takes on a fleshy, tough consistency. The osteoplastic ability may, however, be so great that the destructive character passes into the background. This may be seen particularly well in the bodies of the vertebrae (fig. 641) which become ivory-hard and dense. The order of frequency of metastases is as follows:

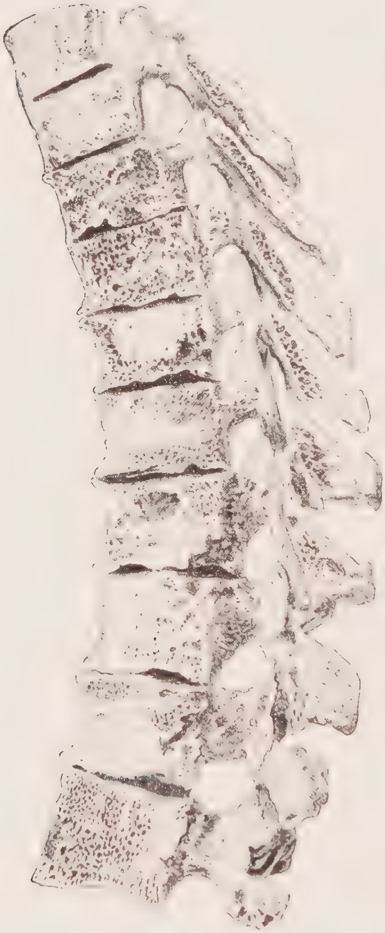


FIG. 641.

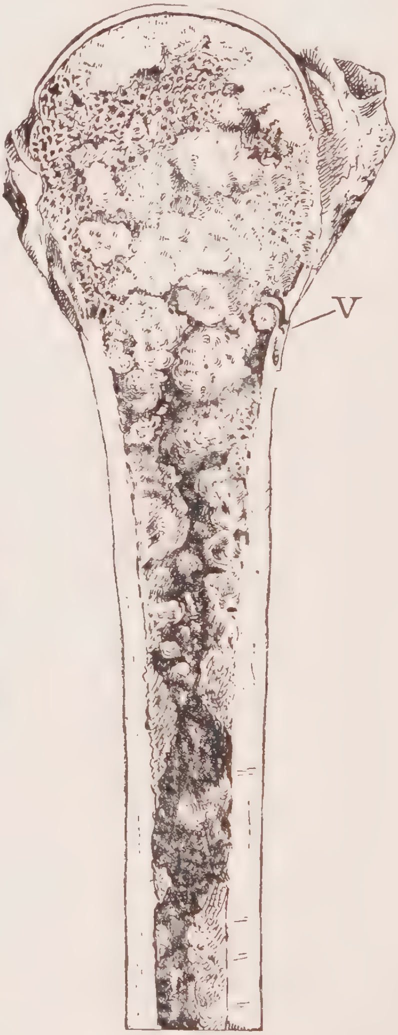


FIG. 642.

FIG. 641.—Osteoplastic and partly osteoclastic carcinoma of the spine from carcinoma of prostate. (figs. 639, 640, 641 drawn from spec. of Collect Basel by W. Courvoisier; Comp. his I. Diss., (Das Prostata Carcinom, Basel, 1901) also the author's, Die malign. Geschw. der Prostata; Socin-Burckhardt, also Deutsch Chir. No. 53, 1902). (V. Thoracic to II lumbar vertebrae); man of 71; ½ nat. size.

FIG. 642.—Numerous carcinoma metastases, ossified, circumscribed, diffuse, in r. humerus of a 48 year old woman operated 2 years before for carcinoma of breast; almost all vertebrae were infiltrated by carcinoma and thickened by osteoid tissue, partly calcified. The femora showed similar changes; V, vas nutriens. Nat. size.

vertebrae, femur (proximal end), pelvis, ribs, sternum, upper arm (proximal end), flat bones of the skull, those of the lower leg, forearm, (v.

Recklinghausen). These bone tumors are often found many years after removal of the primary tumor, particularly carcinoma of the breast, the metastases of which often go into the bodies of the vertebrae, and lead to collapse of the vertebral column, the so-called compression myelitis, and paraplegias. In the material at Basle, among 63 carcinomas of the breast, bone metastases were present 33 times, or 52.3%. Because of the great frequency of breast carcinoma in women, the number of carcinomas of the vertebrae is much more frequent in that sex. Carcinomas of the prostate (more details under this heading), according to v. Recklinghausen and Erbsloh, and the experience of the author (twenty-four cases of prostate carcinoma, 16 showing bone metastases), is next in order to breast carcinomas; nevertheless in the former, metastases may frequently occur in early stages. Both are characterized by an osteoplastic carcinosis. The metastases from carcinomas of the thyroid also strikingly prefer the skeleton (p. 530), (for the variability in their structure, see Emmerich, and also Regensburger); osteoplastic processes are lacking, as a rule, in this case, and furthermore there seems to be a striking preference for the upper half of the body (particularly the skull). Symmetrical arrangement is hardly ever present. The so-called "metastasizing colloid goiters" prefer the flat bones (the sternum, the skull, pelvis). Concerning their histological structure, see p. 533.

The "malignant hypernephromas" of the kidneys very frequently produce early or late metastases in the skeleton; these may be the first clinical symptoms (lit. by Albrecht and Grosheintz), and be mistaken for the primary tumor (see Erdheim). Bony metastases in neuroglioma retinae (Roman) are quite unusual.

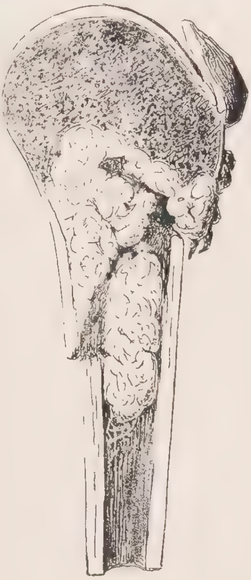


FIG. 643.—Spontaneous fracture (oblique) of l. humerus in metastatic spindle cell sarcoma of uterus of 58 year old virgin. Primary tumor intramural, size of a child's head with rupture as large as the little finger into a vein of the uterus. Many metastases in liver and nodules as large as fists in numerous ribs and sternum; ⅔ nat. size.

In the material at Basle, the author found, in 309 stomach carcinomas, 2.5%, in 159 uterine carcinomas, 5.03%, in 101 carcinomas of the esophagus, 6.9%, in 57 carcinomas of the rectum, 10.5%, bone metastases (I. Diss. Nisnjewitsch), see also Miyauchi (lit.).

Occasionally metastatic bone tumors lead to spontaneous fractures (lit. by Grunert); fig. 643; these may be the first clinical symptom. Infractions also occur. For details concerning the changes in the vertebral column in metastatic carcinomas, and concerning surgical procedures, see Tietze.

Cysts of the Bones.—Bone cysts, usually pseudo-cysts, occur occasionally from softening of former dense tumors, particularly the typical chondromas, more rarely the centrally produced cystic enchondro-fibromas (Schlange). Central fibromas producing internal pressure on the bones, and brown, tough, giant cell sarcomas (Schlange), as well as other sarcomas, callus tumors (Frangenheim), metastatic carcinomas, all may become cystic following hemorrhages, necroses, etc. The first case of this kind of carcinoma was observed by the author in a 46 year old man, with many cystic metastases from a squamous cell carcinoma of the esophagus; see I. Diss. by Tscherniakowsky; see also Lang and Krainz. True primary, or genuine cysts are very rare (lit. by M. B. Schmidt). Cysts appear more frequently in osteomalacia (p. 1071), and particularly often in ostitis fibrosa (p. 1111), in which, as Fujii showed, and Lotsch (lit.) confirmed, liquefaction and disappearance of the fibrous marrow tissue contributes to the formation of the cysts (see opposed, Pommer); in the thin walled diaphysis of a 32 centimeter long humerus, the author saw a 12½ centimeter long, smooth walled cyst, as thick as a thumb with a

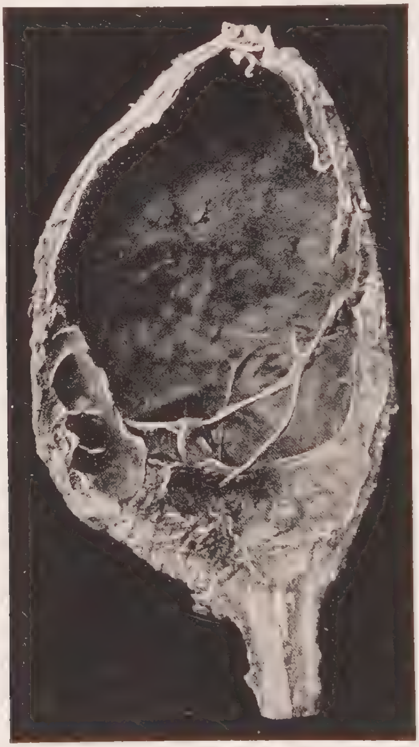


Fig. 644.—Solitary cyst in upper end of r. fibula; circumscribed fibrous ostitis; cyst as large as a fist; man 41 years old. (Fiyii, D. Z. Chir. 113, 1911.)

watery content; cysts also occur in periostitis albuminosa (p. 1102), following dermoid cystomas and cholesteatomas, false, as well as the very rare, true, (see under petrous bone, p. 1105, and under tumors of the soft meninges), as well as from cysticerci (very rare), and echinococci (rare). Cysts may also occur from traumatic causes, inasmuch as hemorrhages produce a secondary rarefying and ossifying osteomyelitis Fujii, lit., Schuster, Duteil, lit., Pommer, (blood sac nature of the cyst); see opposed, the negative experiments of Bolognesi, lit., and Lotsch. Concerning the frequency of jaw cysts, which merit a particular classification because they are true cysts lined with epithelium, see under mouth cavity (p. 586 and forward).

Lit. concerning bone cysts in the appendix.

Parasites of the Bones.—Cysticerci are very rare (Froriep, Bostroem), and unimportant. The echinococcus may establish itself in the long tubular bones (the embryos arrive there via the blood stream), and produce an enormous tumor-like swelling, which is produced just as the shell forming central tumors (p. 1192) and like spina ventosa. But in spite of cavitation of the bone, every sign of swelling may be lacking (v. Bergmann, E. Muller, Frangenheim, lit.), as we ourselves have seen in a preparation of the femur obtained by W. H. Schultze. They occur in the bones of the vertebrae as well as in the flat bones (bones of the skull, rare, Antoniu), in the latter even more frequently than in the long tubular bones (Reich, lit.). The bony tissue is slowly compromised, and, as a rule, shows no reaction (Titow, lit.); the echinococcus may break through the cortex, and spread into the neighborhood. Vesicles may empty through external fistulae (Bauer). The echinococci of the tubular bones (humerus preferred), seem to have the infiltrating habit of the echinococcus multilocularis (fig. 474, p. 974). The entire marrow cavity may be filled with hundreds of smaller and larger vesicles. According to Virchow, it is, however, not a particular form, but merely an echinococcus hydatidosus, the peculiar appearance of which is produced because of its confined development in the preformed spaces between the rigid spongiosa trabeculae (see also Deve). But there do occur, though rarely, true multilocular, small vesicular, bone echinococci, with a typical exogenous proliferation (Abee); Elenevsky and Reich recognize both forms. In the above mentioned case of Schultze, the opened femur showed a connected gelatinous vesicular membrane mass, which filled the diaphysis after having eroded the cortex, and which jutted into the metaphysis; here the echinococcus took on the ordinary appearance of an hydatidosus.

Spontaneous fractures, which, according to v. Bergmann, are the most important clinical signs, may be lacking in echinococcus (Ritter). For echinococci as the cause of pathological luxatio centralis femoris, see under the chapter, luxations.

CHAPTER VI

DISEASES OF THE JOINTS (DIARTHROSES) AND THE SYNARTHROSES

Anatomy.—When we speak of a joint, we usually mean a diarthrosis which is a space between two cartilage covered bone ends, or a cavity called the joint cavity. The first proper idea of the extent and the extensibility of a joint cavity is received when the joint is filled with fluid under pathological conditions, or artificially.

A synarthrosis is union of the bones by means of fibrous tissue, or cartilage, or fibrocartilaginous tissue, without a joint cavity; we speak of a syndesmosis, meaning the ligaments, sutures or seams and membranes between the bones, or of a synchondrosis; false synchondroses consist of union of the bones completed by cartilage or by connective tissue.

Among the diarthroses there are differentiated: (*a*) the ends of the joints; these are bones, covered with avascular cartilage, which in most joints is hyalin, but in others, as for example, the sternoclavicular joint, is fibrous. Along the lateral surfaces, *i.e.*, where the surfaces of the cartilage do not touch each other, the cartilage is covered by perichondrium; this fibro-elastic membrane gradually undergoes transition without sharp boundaries into the parts of the joint free of cartilage and covered by periosteum as well as into the joint cartilage not covered by perichondrium. (*b*) The joint capsules, in which may be differentiated: (1) an external fibrous layer or fibrous capsule of varying strength, and (2) an internal layer intimately connected with the external; it is glistening on its internal surface, moist, soft, pale gray and called the synovial membrane. This, in comparison to other serous membranes, contains tender fibro-elastic tissue in its deeper layers which carries the larger blood vessels; internally, there is a thin layer of parallel, richly cellular, connective tissue bundles, the so-called intima; the smooth internal surface directed toward the joint cavity is covered by a layer of flat cells of endothelial nature which have the ability to secrete, (disputed by Hammar, recognized by Schaffer), and which in situations where the mildest pressure is exerted, are arranged in a number of layers. (According to Braun, these cells are similar to all the other cells of the synovial membrane.) The synovial membrane is folded in many situations; it also contains fibrous synovial tags covered with one or more layers of flat cells; the tags are usually microscopic in size and are particularly thickly strewn along the edges of the joint surfaces where the membrane is attached to the bone; they produce a red silky appearance to the membrane; they contain vessels, *i.e.*, capillaries coming from the larger vessels in the deeper layer, or they are partly avascular. Larger tags may also contain small foci of cartilage which sometimes undergo calcification. The synovial membrane secretes an egg albumen-like, mucoid, viscid, water-rich fluid containing about 6% of solids (albumen, mucin, salt); it is called the synovial fluid. While the cartilaginous ends of the joint are normally free of a synovial membrane, under pathological conditions, the synovial membrane may cover the cartilage with a soft, vascular connective tissue covering (synovitis pannosa).

Particular anatomic characteristics of joint cavities: the joint cavities are closely related to other serous sacs, but show a number of differences. The synovial membranes are characterized from other serous coatings by their thickness, the tags, the richness of vessels, their particular kind of cell covering, (to which cannot be ascribed an independent epithelial importance, Braun), their slimy secretion, which makes them related to all the mucous membranes. According to Braun, the joint cavities must be considered as free tissue spaces bounded by connective tissue surfaces. In pathological relationships, the peculiar situation of the synovial membrane is also important, and is manifested on the one hand by its tendency to profuse, partly serous, partly catarrhal, exudation or transudation, while, on the other hand, the removal of transudates following its poor absorptive ability is rather hindered than increased (Braun), see p. 1233. [For physiology of synovial fluid, see Cajori F. A., Crouter C. Y., Pemberton R., Arch. Int. Med. 37:92:1926.—*Translator*.]

Diseases of the Cartilage in General

Degenerative Changes. In fatty degeneration, fat granules and droplets appear in the cartilage cells. Fatty degeneration may be a symptom of old age, or a local diminution in nutrition, *e.g.*, in inflammations. Superficial loss of substance and ulcers may appear on the surface of the joint cartilages.

Among the changes of old age, the first to be considered is senile softening, seen particularly in the cartilages of the ribs, chiefly in their interiors, but also in the joint cartilages and the cartilages of the synchondroses.

The tissue shows teasing of its fibers, swelling, waviness, molecular destruction, viscid saturation, and finally liquefaction of the ground substance, while the cartilage cells undergo overgrowth, more or less in the form of irregular heaps (not in rows), and are separated from the ground substance by a capsule of a number of layers which is partly doubly refractile; cell masses which lie in the neighborhood of fibrous ground substance take on an elongated form. In the softened places the overgrown cells become more and more fatty, and soon undergo complete destruction; some become free and reach the synovia.

Where the destruction of the fibers of the ground substance begins, there are macroscopic glistening white spots (asbestos-like degeneration), and microscopic, very finely granular, cloudy stripes. Where the process has progressed, and fibers undergo molecular destruction (others may be broken across transversely), the cartilage is macroscopically yellow or brown yellow, transparent (as though cleared in oil), and soft; this yellow destruction of fibers is found on examination of the cross section of the rib in the form of spots or diffuse areas most frequently in the internal parts. Internally, white calcified places are frequently observed. If the cartilage of the ribs is focally dissolved, there appear soft, slimy places, spaces filled with clear fluid, or formed cysts (senile cyst formation). The cartilage cells may contain many fat granules or glycogen drops as well as red yellow clumps of hematoidin.

Ochronosis is a very rare brown to black pigmentation appearing chiefly in the cartilages of the ribs, the joints, the air passages, but also in other fibro-cartilaginous structures such as the intervertebral discs, the pelvis, the intersternal cartilage, the menisci, in mild degree also in the perichondrium and the periosteum, the tendons, the fascias, ligaments and joint capsules, the endocardium, intima of vessels, kidneys, sclera, and the cutis (Virchow). The pinna of the ear becomes blue. The coloring matter (contains sulphur, like some melanins), is in diffuse form or granular. There are differentiated: an endogenous, metabolic disease in some cases surely due to alcaptonuria (Albrecht), and an exogenous form due to chronic carbolic acid poisoning (Pick). In the endogenous forms, particular catabolic products of a changed protein metabolism (homogentistic acid, tyrosin and others), are changed by fermentation into coloring matters. Ochronosis appears usually years after the onset of an alcaptonuria (Ebstein). There also occur alcaptonuric families (Katsch). In the exogenous form which is caused by the repeated administration of small amounts of phenol (over years), these fermentative coloring matters are also formed. The urine of the alcaptonuric (in 32 cases of ochronosis, observed 17 times, Poulsen), becomes dark, and on standing, coal black. Alcapton is identical with homogentistic acid. Allard and Gross produced experimental ochronosis by soaking cartilage in colorless homogentistic acid solution. Many sufferers show chronic, pigmented, arthritic changes, usually in the larger joints. Arthritis ochronotica (Kolaczek, lit.), may be mild, or so severe that it leads to complete disappearance of the cartilage and to ankylosis. Lit. by Heile, Wagner, Landois, and extensive discussion and illustrations by Poulsen, as well as Kolaczek, (lit.), Jantke, Gross. Yellow to dark brown discoloration of the bones—vertebrae, ribs, pelvis, sternum, ossa cranii—of osteohemochromatosis (animal ochronosis, Schmey, lit.), has nothing to do with true ochronosis, but is identical with the hematoporphyria congenita of the human (Gunther, Eug. Fraenkel, Teutschlander).

The spaces which appear in the cartilages of the ribs on softening, may be filled out from the bone marrow or from the perichondrium with vessels and cells. Ossification may occur from this kind of marrow tissue with the formation of spongy bone, or it may turn into fibrous marrow.

Softening of the cartilage also occurs in various chronic joint inflammations. The surface of the joint cartilage becomes silky and papillomatous following tearing of the fibers. If these situations are gradually worn smooth by movements of the joint, there occurs more or less deep loss of substance (ulcers).

Joint capsule ulcers may heal, and the edges of the defects become smooth and covered by a synovial membrane or by an endosteal connective tissue producing a cicatrix (Weichselbaum, Pommer).

Metaplasia of cartilage to mucoid tissue. The cartilaginous ground substance is changed to a mucin-containing fluid; the cartilage cells become branched mucoid tissue cells.

If cells and blood vessels enter this soft mass, it becomes a kind of marrow. Through much transformation into fat cells, it may even take on the character of fatty marrow, or it becomes fibrous connective tissue. This change is partly senile, but may be seen under certain conditions in chronic arthritides.

Amyloid degeneration occurs chiefly in older individuals, and produces a blue yellow spotty condition of the cartilage in the synchondroses and the synarthroses.

Microscopically, the capsules swell unevenly, and take on a hyalin sheen. The cartilage cells also swell and change with the ground substance into a brittle, wavy mass. These situations give the amyloid reaction (p. 948). The author saw the condition occur in elongated ecchondroses of the symphysis of the os pubis, for example, in an 85 year old woman.

Caries and necrosis of the cartilage may be produced by granulating and suppurative inflammations (see under joint inflammation).

Deposits of Calcium Salts and Uric Acid Salts in Cartilage.—The deposit of calcium takes place by preference in previously changed areas, particularly in asbestos-like degeneration. It is chiefly a sign of old age. The edges of the cartilaginous ends of the joints are preferred. The calcium in the form of carbonates and phosphates, is first deposited in the capsules of the cartilage cells, then in the cells themselves, and in the ground substance as a fine, granular dust.

(Concerning calcification and ossification of the pinna of the ear, see Eug. Fraenkel.)

By transmitted light, calcium appears glistening white similar to fat.

For the reaction of calcium, see p. 102. Cartilage which at one time contained calcium removed artificially, stains intensively blue with hematoxylin.

The deposit of urates in the ground substance and in the capsules particularly of the joint cartilages, but also in the cartilages of the ears, etc., takes place in the uric acid diathesis, or gout (see under this disease, p. 1252). The white masses dissolve microscopically into thick bundles of needles and rounded masses. The crystals consist chiefly of acid sodium urates, also of combinations of uric acid with ammonia, magnesia, calcium, etc.

Reaction.—On the addition of acetic acid, the uric acid crystallizes into plates.

The Change of Permanent Cartilage into Bone and Connective Tissue.—Ossification of cartilage takes place frequently as a senile manifestation, particularly in the ribs and larynx, but also following inflammations. The fibrous transformation of hyalin cartilage occurs in various chronic joint diseases, *e.g.*, polyarthritis chronica rheumatica.

During this fibrous metaplasia the cartilage changes into connective tissue, inasmuch as the interstitial substance at first becomes fibrillar, then the capsules disappear, and the cartilage cells become spindle shaped. At the same time there is an hyperplasia, and the cells are gathered in heaps. If vessels enter the substance, and if many round cells appear, the entire picture is that of a granulation tissue.

Hypertrophic and Regenerative Processes in the Cartilage.—Growths of a nodular sort in the joints, composed partly of bone, are seen in the deforming arthritides (p. 1241). These nodules may become loose, free joint bodies. Fractures of the rib cartilage do not heal by cartilage, but by connective tissue or bone; the callus is produced by the perichrondrium. Concerning the union of separated tracheal cartilages, see p. 336. Defects produced by the displacement of portions of cartilage remain practically unchanged, or the regenerative new formation is minimal. Displaced pieces of joint cartilage become either free joint bodies, or, by growth of the synovial membrane, become adherent in some situation or other. Concerning the successful auto- or homoioplastic transplantation of cartilage, see the lit. by Sauer.

Diseases of the Joints (Diarthroses) and Synarthroses

Circulatory Disturbances.—Every joint inflammation begins with acute hyperemia. Often, for example, in the beginning of an acute articular rheumatism, this picture is the dominating scene.

Following marked injection of the vessels, the papillae of the synovial membrane are reddened, voluminous, and much longer.. The synovial fluid may be increased and also thinner than normal.

Hemorrhages into the joint cavities (haemarthros) occur most frequently from traumata; thus following fractures, distortions (particularly knee), luxations, as well as by direct forces, contusions such as pushes, falls, or blows. Hemorrhages into the joint cavities, occasionally also into the synovial tissue, occur in the hemorrhagic diatheses (the so-called blood joints), particularly in the knee and elbow joints, but also in the hip and joints of the foot (Konig, Lossen), but hemorrhages also appear occasionally in severe inflammations (Mankewicz, lit.). (Illustrations by Konig; and also by O. Hildebrand, Allgemeine Chirurgie, III. Aufl. von Konig's Lehrb. 1909. Concerning haemophilia, see also W. Koch, Matsuoka, Sahli.)

If no other severe injuries, and particularly no infectious organisms are present, the serous effusion which follows the entrance of blood into a joint, is usually mild. In the absence of severe lesions of the joints of humans, a large part of the blood may be kept fluid by the synovial membrane for weeks or even months, while in other cases it coagulates in toto quite early; according to Riedel's animal experiments, on the other hand, about two thirds of the blood remains fluid, and one third coagulates. On disappearance of the blood corpuscles, cell strands grow into the coagula, which lie close to the synovial membrane. The free coagula undergo fatty degeneration and disappear completely by resorption. According to A. Israel (lit.) and Bier, the first processes are quite different: the blood soon coagulates, the coagulum becomes smaller in a few hours, and the effusion looks as though it had been that of fluid blood. The coagulum is dissolved by the synovial membrane, the fibrin is decomposed, joint fluid is added, the erythrocytes which have not been dissolved with the coagulum, give an appearance as though the blood had remained fluid. The resorption of an hemorrhage occurs in general quite quickly, but, for example, in the knee joint, in spite of a seeming regression, healing takes place only after weeks. If resorption is hastened by tears in the synovial membrane, (v. Volkmann), the blood runs through the tears and is absorbed. According to Braun, this indicates that the synovial membrane not only does not possess marked resorptive ability, but actually hinders and slows absorption. (See also A. Israel.) It is of practical importance that after hemorrhage into a joint (years later), there may remain yellow or rust brown pigmentations, produced by the deposit of hemosiderin. In a hemorrhagic joint, the papillae become brown. In rarer cases, following organization of the hemorrhage and tearing apart of the cartilage, there develop adhesions of the joint walls and stiffness (ankylosis); this may also occur in a blood joint.

The Acute and Chronic Inflammations of the Joints.—In a joint inflammation, the synovial membrane is often the chief part involved. In other cases, and this is true of most forms of chronic arthritis, the remaining parts of the joints are also attacked. The first type of joint inflammation is called synovitis or arthromeningitis, the second panarthritis or merely arthritis.

According to the anatomical characters displayed by the acute inflammation in which, practically without exception, there is considerable exudation, there may be differentiated: a serous, or sero-fibrinous, a fibrinous, a suppurative, a sero-purulent or a sero-fibrino-purulent form. In the chronic inflammations, which show more anatomic forms than the acute, two main groups may be differentiated: arthritis exudativa (serosa and purulenta), and arthritis sicca, according to whether the formation of a free exudate into the joints has taken place or not. The separate anatomic and etiological forms of chronic joint inflammations will be discussed later. The specific infectious joint inflammations will also be discussed under separate headings.

The Exudative, Acute and Chronic Inflammations of Joints.—The inflammation in a joint is soon localized, and often exclusively, in the synovial membrane. This shows injected vessels, thickening of the folds, waviness, and may look like a vigorously reddened mucous membrane; it produces an exudate. If the inflammation is of some duration, the papillae grow, and the synovial membrane swells out over the cartilage.

In arthritis or synovitis serosa (hydrops articulorum acutus, hydarthros acutus), considerable serous transudate soon appears and swells the joint, as for example, after contusion of the knee joint, or, the exudate is less in amount, as for instance, in acute joint rheumatism. The fluid is yellow, lighter and thinner than the normal synovial fluid. It is frequently mixed with tiny yellow fibrinous flakes and the condition is then spoken of as arthritis serofibrinosa.

The course: acute serous synovitis, the mildest form of joint inflammation, may regress spontaneously in a short time, *e.g.*, if of traumatic origin; or, there is a tendency to recurrences, and from this there may develop a chronic hydrops of the joint; this occurs particularly frequently in the knee. A chronic serous joint inflammation, hydrops articuli chronicus, may, however, begin insidiously. The amount of fluid is often extraordinarily great; it is rich in albumen, and either much thinner than the synovial fluid, or much thicker, and gelatinous, and shows microscopic cells of the synovial membrane and granules. Fibrin clumps are also met. If dense rice bodies are found in large numbers, the condition, as a rule, is tuberculous. Severe anatomic changes need not occur for long times, but in a hydrops of long standing they are seldom absent. The synovial membrane may become thickened and cloudy, the papillae may enlarge and become red nodules as large as the head of a pin, or they may undergo more vigorous growth in the form of soft, flat, papilliferous masses all over the cartilage (arthritis or synovitis pannosa s. synovitis prolifera).

At the same time the cartilage shows changes around its edges, such as overgrowth, fatty degeneration, and shredding, as in arthritis deformans. The outer layers of the capsule may become thickened. Anomalies of position and flail joints may result.

In hydrops of the knee, the enormous bursa, particularly the subcrural bursa, is also distended. When the fluid is large in amount, "the patella floats," the knee joint appears as though artificially injected. For the difference in the external shape of the joint in empyema, see p. 1236.

Acute fibrinous joint inflammation, as a rule, is combined with considerable serous exudation. White fibrin flakes are found in the exudate, or fibrinous membranes cover the joint cartilage. The very rare, quite dry, fibrinous synovitis (fibrinosa sicca), which occurs without serous effusion, readily leads to chronic joint changes; by organization of the fibrin masses, adhesions are produced with the synovial membrane and among each other. Changes in the cartilage, obliteration of the joint cavity, may follow (consult under chronic adhesive arthritis, p. 1249).

Suppurative joint inflammation which may occasionally take on an ichorous character, *e.g.*, in gun shot wounds of a joint, may be differentiated into two chief forms: (1) synovitis purulenta, suppurative catarrh, blennorrhea of the joint (v. Volkmann), joint suppuration, exudative joint empyema; the synovial membrane infiltrated by cells, secretes pus; (2) suppurative panarthritis, which may appear independently, or develop from a chronic synovitis purulenta. All soft parts of the joint, and the entire capsular apparatus are involved. The condition is also known as capsule phlegmon (Payr). This is an actual joint suppuration; destruction of the joint and paraarticular phlegmons are usually the results.

In these severe forms, the synovial membrane undergoes progressive suppuration; the cartilage shows cloudiness, shredding, softening, fatty degeneration, ulcerative destruction (caries), and necrosis. If the bone is laid bare after destruction of the cartilage, the pyogenic organisms may produce suppuration in the marrow cavity with resulting caries and necrosis of the bony joint ends (p. 1104). More frequently, vice versa, a joint suppuration is secondary to a process in the bones; see for example, under osteomyelitis, p. 1101. If the external parts of a joint and their surroundings are attacked, there appears a diffuse peri- and paraarticular phlegmon, often with coincident collateral edema, or circumscribed abscesses in the neighborhood of the joints which may perforate externally. Occasionally gravity abscesses are produced, as for example, in the musculature of the calf following knee joint suppuration. Whereas in marked hydrops genu, the contours of the over-stretched joint cavities are recognized with their recesses, just as though the joint had been filled artificially to its maximum, these contours are washed away in empyema of the external surroundings.

Results.—Restitutio ad integrum is still possible in a suppurative arthritis, as long as it does not become more than an acute suppurative catarrh (v. Volkmann); the pus is destroyed and absorbed. After destruction of the cartilage, the marrow tissue undergoes suppuration, shows vigorous granulation tissue formation with a tendency to ossification (Tashiro), and thus situations denuded of cartilage may undergo sclerotic bone formation. If the condition is not very extensive, so that sufficient cartilage remains, the movability of the joint need not be seriously disturbed. More frequently, however, the result is less favorable, particularly if the course is chronic; then there are shrinking and shortening of the joint capsules and incomplete ankylosis; when the soft parts are involved, or when the cartilage and the bones are also attacked, the result is complete ankylosis. This consists either of fibrous adhesion, or bony union of the ends of the joints. Occasionally a vigorous periosteal bone growth leads to the formation of irregular, angular, thickenings, external to the joint, whereby a bony bridge ankylosis is brought about. In coxitis, protrusion of the floor of the acetabulum may lead to narrowing of the pelvis (Breus and Kolisko).

Etiology of the Exudative, Acute and Chronic Inflammations of the Joints.—Primary and secondary joint inflammations may be differentiated.

Primary arthritides may be produced by traumata, gun shots wound, crushes, tearing; they are almost always combined with hemorrhage ints the joint, and may give rise to a serous, fibrinous, suppurative, or ichorouo inflammation. Other primary arthritides occur by hematogenous routes and are usually of infectious origin. The most important form is acute articular rheumatism (rheumatismus articulorum acutus, polyarthritis rheumatica), a febrile infectious disease (a pyemia of diminished virulence), with unknown portal of entry, but perhaps from the tonsils (Pickenbach) and the pharynx, and with a bacterial cause which has not as yet been demonstrated with certainty (Suchanneck); according to P.

Meyer, it is a streptococcus infection of a particular kind; according to Vetlesen, it is caused by pyogenic cocci in general (which produce an ordinary angina); for the development of an articular rheumatism, it is said, however, that there must be added an individual reaction (for other views, see Weintraud). In about one-fourth of the cases, it involves the endocardium, and the myocardium as well as the joints. Fahr recently described a noteworthy formation of connective tissue nodules in the synovial membranes, which, together with periarticular nodules (p. 64), in spite of certain histological differences (lack of giant cell formation), he believes are equivalent structures to the rheumatic nodules of Aschoff. This extraordinarily painful disease usually jumps from joint to joint, but the swelling need not be excessive. The character of the exudate, which, as a rule, is small in amount, is usually serous, but is occasionally fibrinous or even suppurative. The disease may appear as a local epidemic. See the work of Pichler, lit., concerning the very severe changes in the upper cervical vertebral column in acute joint rheumatism which may be difficult to distinguish from tuberculosis. [For studies of a bacterium in rheumatic fever, see Small, J. C., Am. J. Med. Sci. 173: 101: 1927.—*Translator.*]

Primary suppuration of a joint may also occur in acute osteomyelitis (pp. 1095, 1096); but more often it is secondary to this condition.

Secondary arthritides may be extensions from the neighborhood, following an osteomyelitis, an ichorous periostitis, phlegmons, or an ichorous process in the neighborhood. Thus, for example, in puerperal sepsis, a number of joints in the pelvis may undergo acute ichorous inflammation, whereby wide open relaxed separations are produced. An encapsulated osteomyelitic focus in which staphylococci remain latent and virulent for even five years may produce recurrent joint hydrops over a period of years (Garre). Tumors in the bones or joints may also produce exudation into the joint cavity. But secondary joint inflammations occur more frequently by the hematogenous route as metastases of an infectious disease. The metastatic arthritides are ordinarily suppurative or ichorous. Bacteriologically, the organisms of the primary disease or its complication are found in the exudate. When the suppurative or ichorous exudate is removed, the joint cavities may show very little or no changes. As points of origin may be considered: pyemic processes, *e.g.*, puerperal infections or a septic phlegmon which may occur from infection during autopsies, typhoid fever (lit. Ellis), dysentery (Dorendorf), cerebrospinal meningitis, erysipelas, scarlet fever (only when complicated), measles (rarely, Fritsch), gonorrhea, pneumococcus infections (Zesas, Kaumheimer). Mild, but often very obstinate arthritides are quite frequently observed in the course of a dysentery (lit. by Chiari).

Gonorrheal inflammation of the joints occurs most frequently in the knee, after which, in the joints of the foot, the hands, the fingers, and the toes; it is often combined with inflammations of the tendon sheaths (in the feet and hands), and also, but more rarely, with inflammations in the bursae. The condition is particularly frequent in large cities. The metastases of mucous membrane gonorrhea (not only from the genitals, but also from a blennorrhoea conjunctivae, stomatitis neonatorum, etc.; see under gonorrhea), into a joint, may appear first after the original gonorrhea has been present months or years, and in women, in which it occurs not rarely during pregnancy or in the puerperium (Konig), it is perhaps more frequent than in men (D. Nasse). It also occurs in children (Emmet). Traumata are important in the localization. In women, the joints of the hands are involved particularly often. The condition may be mono- or polyarticular. The joint which is involved first is usually very painful, more so than in acute articular rheumatism. Clinically, forms may be distinguished with and without exudation; the former are the more serious, and the para- and periarticular tissue is the chief site of the exudate; a transudation may or may not take place into the joint; the latter form is seen occasionally in the course of a tuberculous tumor albus which looks quite similar. The quality of the exudate is serous or suppurative (grave, serious prognosis). Gonococci may be obtained in pure culture (Bauer). For statistics concerning gonorrheal arthritis, see Jordan; concerning metastatic gonorrheal diseases, see lit. by Nobl.

The Chronic Joint Inflammations Which Proceed without Exudation or with Mild Exudation.—If we except the specific infectious (tuberculous and syphilitic) arthritides, as well as gouty arthritides, these include a number of changes which have been grouped under the general designation of "arthritis deformans," because the chief weight has been laid upon the deformities produced in the joints, and also because clinically the forms cannot easily be differentiated. But from the anatomical point of view, the conditions may be divided into a number of categories; some are of inflammatory nature, some are primarily regressive and involve chiefly the cartilage, and are caused by wearing away, senility, trauma, or nutritional circumstances; but these various sub-groups often show transitions, and etiologically the grouping cannot as yet be made uniform.

According to anatomical criteria we may differentiate two chief groups, and three chief types.

Arthritis (osteoarthritis) **chronica deformans;**—degenerative changes of the cartilage are primary; secondarily there appear atrophic processes in the bones with vigorous growth in the joint tissues such as from the cartilage, the bones, the synovial membranes, and the capsules. The condition may be poly- or monarticular.

From the etiological-pathogenic viewpoint we may differentiate:

(*a*) Primary arthritis chronica deformans; usually polyarticular;

(*b*) Traumatic arthritis deformans; primary traumatic cartilage ulceration and subchondral disturbances lead to a secondary arthritis deformans, as a rule, monarticular. The deformities may reach very high degrees, especially because of marked hypertrophic changes, (fig. 645).

Arthritis chronica ulcerosa sicca; the progressive processes are degenerations in the joint cartilage. In this category must be placed the so-called malum senile (coxae) which usually involves one joint and is a form of senile arthritis, while other senile arthritides are polyarticular (Steurenthal, Beitzke); the latter are probably merely quantitatively different from the former. There are also transitions from a to b. Pommer's opinion agrees with this classification. The contrast often made between the hypertrophic form, *i.e.*, the ordinary arthritis chronica deformans, and the atrophic form with the picture of malum senile, is therefore purely external, since the processes are alike in their fundamentals. Malum senile is a localized form of arthritis deformans.

Arthritis Chronica Adhaesiva.—Inflammatory changes of the soft parts of the joints, particularly the synovial membrane, are the beginnings of the process. Later this form is characterized by replacement of the cartilage with connective tissue and adhesions of the opposing joint surfaces. The chief representative is chronic polyarticular rheumatic arthritis.

For more details concerning classification and the nomenclature of the chronic arthritides, in which there is much confusion, see the lit. in appendix. Extensive lit. concerning arthritis deformans by Pommer. A review of the functional theory of Pommer has been written by v. Stubenrauch, the microscopic findings by Weichselbaum.

Arthritis (Osteoarthritis) Chronica Deformans.—It is characterized by the fact that the primary degenerative processes in the cartilage have added atrophic processes in the bones, and extensive hyperplastic overgrowths of the entire joint tissues.

The changes in the joint cartilage begin with degeneration which leads to teasing apart, lifting and softening. While the cartilage cells undergo vigorous growth and at first produce large foci ("incubator capsules" with a number of cells; fields of proliferation, Weichselbaum), the ground substance becomes more and more teased apart and liquefied; then the liquefaction proceeds in the tissue, particularly in the depths in the layers close to the bone, with fatty degeneration of the cells and myxomatous destruction of the ground substance. This produces softening cavities in the cartilage. Changes in the bones are produced subchondrally, and will be discussed in more detail below.

Thus in focal situations, at first in the positions where the movement of a joint produces the most marked pressure, there is complete disappearance of the cartilage. These situations are occasionally covered by growing synovial membranes; more frequently, however, the bones are bared.

Pommer described healing processes, whereby defects in the cartilage are closed by synovial growths and by membranous structures. The author has also seen such conditions.

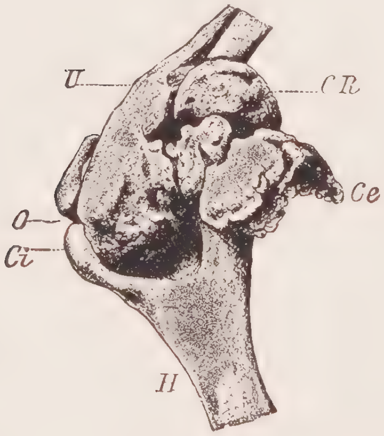


FIG. 645.

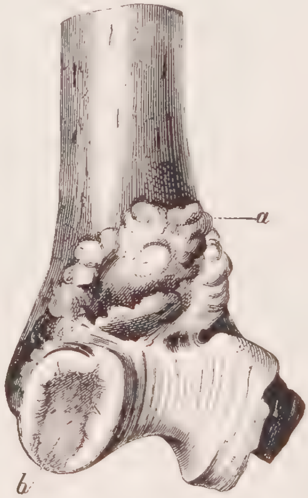


FIG. 646.

FIG. 645.—Monarticular intense deforming arthritis (traumatic) of left elbow joint with almost right angled ankylosis; from a woman of 52; H, humerus; Ci, internal condyle; Ce, external condyle; U, ulna; CR, fungus-shaped head of radius; O, olecranon. Between CR and Ce, a free joint body, above Ci, a so-called free body in the joint capsule.

FIG. 646.—Beginning arthritis deformans at lower end of humerus; a, osteophytes; b, grinding surface of bone, surrounded by marginal ridges. (Billroth's Allg. Chir.)

The uncovered bone becomes more dense by way of a sclerosing fibrous ostitis which comes from the marrow cavity from apposition of the bones in the older trabeculae; it becomes polished by the joint movement, and appears brown yellow and glistening like porcelain. This grinding produces gutter-like lines, particularly when the joint movements are hinge-like, as in the knee.

The more marked the rubbing, the more vigorous the subchondral new bone formation, whereas in situations where the rubbing is permanent but mild, or when atrophic situations are rubbed, the bone becomes porous. These porous spaces become filled partly with fibrous marrow, partly with vigorously growing, but shredded cartilage (Walkhoff).

Further changes are (1) growth processes, and (2) atrophic, resorptive processes. In (1) there may be differentiated myelogenous (particularly around the edges), and periosteal (osteophytes) activities. The growths around the edges merit the chief interest. In the marginal parts of the joint cartilage there arise flat, ecchondrosis-like protuberances which often produce a sort of crown (fig. 646 under b). These wavy outgrowths, called border growths by Pommer, which have been compared to poured and hardened plaster of Paris, bespeak the character of the entire affection according to v. Volkmann, who believes they are ossifying ecchondroses. In addition to that, however, there are also periosteal osteophytic growths, which likewise are rounded, flat, often very dense, nodular deposits, but established external to the cartilaginous joint surfaces on the external bony surfaces (as in fig. 646 under a). Both kinds of outgrowth frequently reach considerable size, and contribute to the deformity of the joints.

These marginal growths are subject to many different interpretations. They were early considered ossifying ecchondroses (v. Volkmann), or ossified perichondral structures (Nichols and Richardson), or osteophytes, or even eversion of the margins (Ziegler, Kimura), which arose through the sinking in and the bending of the primarily atrophic corticalis of the lateral surfaces of the joints.

Pommer first showed that these growths arise from the subchondral marrow tissue, and consist of lamellated bony trabeculae of the bone upon which they are placed, and are covered by the superficial layers of the joint cartilage. After the removal of the protection exerted by the elastic cartilage against mechanical influences, there is a reactive bone overgrowth from the marrow; the entrance of vessel buds and marrow spaces, in the extensively dissected cartilaginous joint covering and the lamellated bone formation, helps the ossifying outgrowth, which still possesses a covering of resisting joint cartilage. This cartilaginous layer is, however, not normal. "Fields of proliferation" (p. 1239), may produce chondrogenous growths of local character as ecchondrosis-like protuberances. Pommer believes these ossifying marginal growths are the most important in the diagnosis of arthritis deformans.

(Fromme believes they are attempts at regeneration, to replace the lost tissue.)

The resorption processes consist of lacunar bone disappearance. Furrow-like concavities, (resorption ulcers), appear here and there, and with the ulcers produced by grinding, lead to gross changes in form; the heads of the joints become smaller and flat, as in a compressed plastic mass. The bone marrow which takes the place of the disappeared trabeculae, becomes lymphoid, or gelatinous, or fibrous; it may also undergo liquefaction, whereby cysts filled with fluids appear. At the same time, new cartilage and bony trabeculae are formed in the cellulo-fibrous marrow.

The subchondral changes in general are very varied. We have mentioned those of the marginal growths. Then, as Pommer demonstrated, there appear complex reactive overgrowths following kinks and splintering, breaks and bends in the subchondral bony cortex. This leads to hemorrhages, cell and tissue overgrowth, which Kimura and Walkoff compare to callus. Among these various pictures, Ziegler has pointed to one which he calls "recartilagination" believing it is a reappearance of cartilage in osteoid trabeculae which enter into the marrow spaces as ecchondrosis-like excrescences; but Pommer could show the opposite, *i.e.*, the result of separation in the continuity of the border between the cartilage and the bone, is that the uncalcified, deeper layer of the cartilage gives up cells which are carried by way of the lymph channels along the bony trabeculae and the marrow vessels into the bones lying under the unchanged or changed joint surfaces, and here they grow out into numerous cartilaginous nodules reaching deep into the spongiosa spaces. (In traumatic arthritis deformans, this latter process is said not to occur.) The cysts which are also observed, and which Ziegler believes are due to softening, have been shown by Pommer to be encapsulated hemorrhages (see above), or due to splinters in masses of detritus which act like corks in the marrow cavities; others describe them according to their content as cartilaginous debris cysts. (See the characteristics of these changes in illustrations by Pommer.)

In determining the importance of the atrophy, the mechanical point of view is important, namely, that parts not exercised become atrophic (Walkhoff). It must, however, be taken into account that typical arthritis deformans usually develops in older individuals, who, at that time of life, have general osteoporosis. In the origin of the subchondral processes, (infractions, etc.), and the complex affairs which follow (carrying away of cartilage, cyst formation), the wide meshes of the compacta are undoubtedly a big help. Kimura believes the important point in the genesis of arthritis deformans is the bone atrophy, but, on the contrary, the author, Walkoff, Beitzke, believe that the cause of arthritis deformans is degeneration of the cartilage. Axhausen then called attention to the importance of aseptic necroses of the bone and cartilage (necrosis theory), maintaining that they were definite irritants to bone and cartilage overgrowth; these necroses are said to come from traumata, inflammations, disturbances in nutrition (old age, lues, alcoholism, etc.). Wollenberg's vascular theory postulates a local discrepancy between the arterial supply, which is insufficient and hence produces undernutrition because of arteriosclerotic narrowing, and the venous outflow which produces overnutrition from venous stasis, both of which conditions can explain both the regressive and the progressive changes. This theory has been abandoned by

Axhausen, Walkoff-Ewald-Preiser, etc. According to Preiser's static theory, irregularities or misfits in the joint surfaces produce strain and uncovering of the borders of the joint surfaces, and this leads to arthritis deformans. Disagreeing with all of these theories, Pommer, in extensive investigations, suggests a functional theory, as inaugurated by Beneke (p. 1246), and developed further by Walkoff. The cartilage produced in amounts above the physiological need suffers in its elasticity, which finally is abolished. The results of this primary cartilage degeneration are secondary overgrowths in the subchondral marrow spaces, and vascularization and ossification of the previously changed cartilage lying over these spaces. These disturbances of nutrition and the changes which diminish the elasticity of the cartilage, occur in overexertion, *e.g.*, in certain occupations such as scrub women, bakers, lock-smiths, in workers in general (Beitzke, Preiser, Pommer and others). Many believe that pure functional damage does not explain the susceptibility of the cartilage, and suggestions of humoral influences have been made in the form of chemical alterations in the cartilage (Ledderhose, lit.), thus, from a toxemia from the intestinal canal, or influences of the thyroid gland, etc. It has been stated that thyroid extract produces a favorable influence in arthritis deformans (Longmead). Probably thermic influences (change from cold to warm, etc.), are of some importance (v. Manteuffel).

The joint capsule also takes part in the growth. In severe cases, the bands and folds thicken, while the synovial membrane undergoes overgrowth, particularly at the transitional places. The papillae are lengthened, show outgrowths, and produce a fringe-like attachment to the edge of the cartilage which sometimes becomes covered by the cartilage (synovitis prolifera). A characteristic finding is the absence of fluid accumulations (v. Stubenrauch). The tendons and muscles occasionally participate in the new bone formation.

If the preexisting papillae undergo growth (H. Stieda), and if the fatty tissue previously present or grown into the parts (subsynovial) produces arborescent papillae, the condition is known as lipoma arborescens (particularly around the knee joint), but it is no tumor in the narrower sense of the word. Exceptionally the lipoma is solitary about the knee joint (v. Stubenrauch), but in the form of a true tumor. Papillae may be snared off, and become free joint bodies. (Lipoma arborescens also occurs in tuberculosis.) The papillae in a synovitis occasionally contain cartilaginous foci (synovitis prolifera cartilaginea), which may undergo central ossification, become free, even though quite large, and give rise to numerous joint bodies or joint mice (fig. 663); other joint mice originate from the breaking off of particles of the ends of the cartilage or from border exostoses (details by Barth, Hahn, Kappis, lit.). The so-called rice bodies (p. 1257), occasionally occur in important numbers. It is only exceptional that there is much serous transudate into the joint cavity (see above).

Another form of joint disease has been called arthritis chronica villosa (Schuller), which is confined merely to the synovia of the joint. There are connective tissue overgrowths, perhaps also fat tissue (lipoma arborescens). For chondromatosis (Reichel), see under tumors, p. 1262.

Fasciitis palmaris, in advanced stages leads to the so-called Dupuytrens finger contraction; it is believed by Ledderhose, to be a constant accompanying symptom of arthritis deformans.

Inasmuch as the described changes consist of both disappearance and overgrowth of cartilage and bone, mechanical forces may produce luxations, infractions and breaks during the movement of joints, and lead to changes in their configuration.

Monarticular traumatic arthritis deformans (p. 1239 and fig. 645), is often a joint body disease (Kappis, and p. 1246).

The reason why ankylotic adhesions do not occur more frequently in arthritis deformans in spite of the laying bare of marrow spaces and vascular tissue, is believed by Pommer, to be the continuation of functional activity, *i.e.*, of joint movements.

The head of the femur may show different appearances, become elongated or cylindrical, because of the addition of border exostoses which produce marked thickening; in other cases it is shortened, broad, fungus shaped, or quite flat, as though it had been hammered (fig. 647); combinations of disappearance above, and replacement at the lower edge, makes it appear as though pushed downward on the shaft; it reposes directly on the diaphysis without a neck, or it is sunken deep under the rim of the greater tronchanter. The head fits into the socket, but the normal movements are hindered by other conditions. In so-called wandering of the acetabulum, the socket is dilated, the old edge atrophies and disappears, while a new one replaces it from the periosteum. This rearrangement of the socket may shorten the leg as a whole. The head of the femur is occasionally subluxated upward if the capsule becomes relaxed, or the overgrown edge of the socket may so surround the head of the femur that it cannot be brought out of the acetabulum, although it is still somewhat movable. In elongated cylindrical heads, movement is possible in only one direction (extension and flexion). But the joint as a whole may become entirely stiff (deformity ankylosis), a result sometimes occurring in other joints such as the elbow (fig. 645). The knee joint (fig. 594), frequently becomes unstable and flail-like, produces deformities such as genu valgum or varum, subluxations, contracture positions, with marked hindrance to its movability; when the ends of the joints are flattened and broadened any sort of movement is impossible. An incarcerated mouse can produce sudden painful inhibition of movements of a joint (the mouse symptoms of the surgeon).

In spondylitis deformans (fig. 647), the intervertebral discs become inelastic, pressed flat, and squeezed out. Periosteal overgrowths produce clothes pin- or bridge-like ankyloses. These bony bridges are usually laid over the anterior lines of the vertebral bodies, which often show senile osteoporosis, are flattened, and have led to a tendency to kyphosis (usually to the right); occasionally there are merely eaves- or balcony-like supracartilaginous exostoses, which communicate with another, or the growths of the upper vertebrae lie like shingles on those below. In other cases the anterior aspects are covered by a communicating bony icing. Even the anterior longitudinal ligament may undergo ossification, and the small joints likewise become ankylosed (Simmonds). In fact, the entire vertebral column may become more or less completely ankylosed (according to Eug. Fraenkel, scarcely ever in toto), and thus finally become kyphotic. More often, it is merely one part, the lower thoracic, lumbar, or cervical region, which is totally stiff, crooked or bowed laterally. Even though older writings emphasize the functional role of the cartilage in arthritis deformans (Rokitansky, Weichselbaum), it was Beneke, sup-

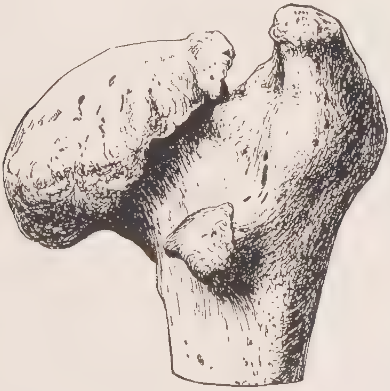


FIG. 647.

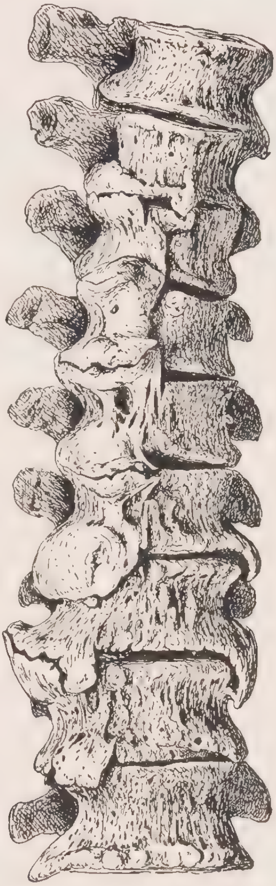


FIG. 648.

FIG. 647.—Arthritis deformans; r. femur, posterior aspect. The fungus-shaped, much flattened head with smoothly polished articulation surface and lumpy bone proliferations on overhanging margin appears as though it had slipped downwards; neck much shortened Above, very hard osteophytes on greater trochanter and on the fungus-like lesser trochanter.

FIG. 648.—Spondylitis deformans of porous lower thoracic and lumbar vertebrae with light kypho-scoliosis and sclerotic bridge-ankyloses; about ½ nat. size.

ported by Fraenkel and Simmonds, who first recognized the beginning of the process in diminished elasticity of the intervertebral discs; the characteristic new formation of bone, consisting of rearrangement of the older spongiosa and bony enclosure of the intervertebral discs, is due to mechanical influences, not pressure, but concussions, which produce a functional thick bone deposit in those particular situations, because of the lack of the elastic pillows. Thus spondylitis deformans is a chronic, painful disease which produces a stiff vertebral column and more or less diminution in its movements. If the intervertebral foramena are narrow, root symptoms (radiating pains, atrophic, usually incomplete, paralyses) are added. It must be remembered, however, that ordinary contusions of the vertebral column in the direction of its long axis, such as from falls on the buttocks, may occasionally, among other things, produce these bridges along the anterior edges of the vertebral column because of callus formation (Quetsch, Payr and Kreuzfuchs).

Ankylosing Spondylitis.—The anatomical picture differs from that of spondylitis deformans; it is characterized by chronic stiffening of the vertebral column with bowing, (Bechterew), often in conjunction with ankylosis of large joints, the "roots of the limbs" (spondylose rhizomelique, P. Marie), particularly the hip, less commonly the shoulder (type P. Marie-Strumpell), in younger individuals, particularly those of "rheumatic" type, or in those with chronic infections (particularly typhoid, Eug. Fraenkel), or toxemias (P. Marie and Leri), or subject to changes of temperature; traumata are also important. Isolated vertebral bodies are not deformed, in contrast to spondylitis deformans, but the entire vertebral column, if the disease is of long duration; bony bridges may develop in either disease. (For x-ray differentiation, see Schlayer.) Siven and Eug. Fraenkel (lit.), Rumpel, and others, believe that both the point of origin and the severest lesions are in the joint capsules of the processus articulares in the form of an ulcerating and ankylosing disease of the joint surfaces, a condition known as arthritis chronica ankylopoetica (see p. 1249). The joints between the ribs and the vertebrae may disappear, (according to Hoffmann, lit., also small peripheral joints). On the other hand, Simmonds believes the most important feature is ossification of both the ligaments and tendons of the vertebral column, not only of the joints themselves, but of those which do not belong to the joints; Ehrhardt (lit.), postulates a "syndesmogenous synostosis" of all the vertebral joints with ossification of the lig. flava and partial ossification of the intervertebral discs. But in a further communication, Eug. Fraenkel emphasizes that it is a primary arthrogenous disease (Wehrsig). Marie and Leri believe spondylosis rhiz. begins as a rarefaction of the bones, which then produces a secondary reactive (quasi curative) hyperossification of the ligaments, the tendons and the menisci.

Arthritis deformans may be poly- or monarticular, in either case a primary disease. Thus, in malum senile usually but one joint is involved (hip, knee). Secondary monarticular arthritis deformans is often traumatic in origin, and usually attacks a larger joint of healthy individuals (fig. 645). These joints are usually non-painful. Among the traumata may be considered repeated contusions, distorsions, and fractures, particularly those which penetrate the joints. The deformities may be of the highest degrees. But more frequently a trauma produces chronic serous synovitis, if hemorrhagic, an adhesive arthritis; the same occurs after replacement of a luxation. But in joints luxated for a prolonged period of time the result is frequently a deforming arthritis. See v. Sury, lit., Kohler.

Sometimes an infectious arthritis, as a chronic hydrops or a chronic suppurative catarrh of the synovial membrane, does not produce destruction of a joint, but does become an arthritis deformans, whereas ordinary destructive joint inflammations usually produce adhesions and ankyloses. A tuberculous arthritis with synovitis, has been known to assume the appearance of arthritis deformans.

Polyarticular forms are more frequent in women, usually after their thirtieth year; the etiology is obscure, but it is thought that there is a nervous basis; it occurs more often in the smaller joints, particularly those of the hands and feet, but larger joints are not entirely exempt. The joints crackle and crepitate on movement, the surrounding muscles undergo a certain degree of atrophy, so that deformity of the hands, for instance, may be very important and highly characteristic.

Arthritis Chronica Ulcerosa Sicca.—So-called malum senile is merely a gradual localized form of arthritis deformans; its chief differential point is the predominance of regressive atrophy of the cartilage—in which the process, as in arthritis deformans, begins with shredding of the ground substance and fatty degeneration of the cells, while overgrowth processes (edge growth) are present to only slight degrees. The bone laid bare by ulceration of the cartilage is, and often remains, porous, even though a porcelain-like sclerosing of certain parts takes place, *e.g.*, in the head of the femur. The periosteal bone overgrowths are also unimportant. These changes, as a rule, are indefinite. To be strictly formal, we might possibly call the condition arthritis deformans atrophica (Beitzke and others). Both diseases, viz., arthritis deformans and malum senile, are but different in degree; there are transitions from one to the other; perhaps all the difference is due to the senile character of the tissues, for the disease is, as the name states, one of senility.

Ordinary chronic arthritis deformans occurs as a senile disease, although not necessarily. We have seen that marked reactive overgrowth is not hindered by pure senility. But in malum senile, particularly severe senility of the tissues cannot start these reactions, or, if started, they progress to only mild degrees.

It is most frequent in the hip joints and the knees, but may occur in the shoulders, elbows or fingers. Secondary muscle atrophy in the latter may produce deformities and subluxations, (fig. 649). (See Stempel, who calls attention to wide differences in these late stages of malum senile and typical arthritis deformans.)

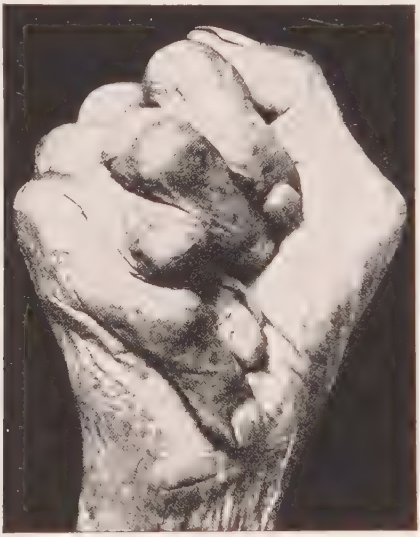


Fig. 649.—Arthritis deformans (malum senile) of finger joints of r. hand of a woman 88 years of age. During life the deformed fingers were almost immovably fixed in this position.

Joint diseases also accompany certain conditions in the central nervous system; the form may be similar to that of arthritis deformans, but the atrophic processes are very marked. See under neuropathic arthropathias (p. 1250).

A condition named arthritis coxae juvenilis by Perthes, and later called osteochondritis deformans juvenilis, is different from the arthritis deformans of adults; in the former condition, usually in boys, the upper epiphysis of the femur disappears. There is a great difference of opinion concerning the origin. Perthes hypothecates a number of causes which lead to occlusion of the artery of the neck of the femur and thus initiate the process. Others lay stress on trauma, others on rickets or late rickets, others on developmental disturbances of the epiphyseal line, and even a staphylomycosis has been hypothecated by a number. Perthes himself arrives at the conclusion that very little has been demonstrated as yet. (Lit. by Calve, Nieber, Fromme, Frangenheim, Levy, Brandes, Kreuter, Zaaijer and lit. in appendix.)

Arthritis Chronica Adhesiva.—Inflammatory changes in the soft parts of the joints (synovial membranes and the capsule with periarticular tissue), are the primary conditions. This leads to connective tissue growth in the shredded cartilage which is invaded by blood vessels and cells from the growing synovial membrane. The latter covers the joint cartilage (arthritis pannosa), and burrows into it from above downward. In arthritis deformans, on the other hand, vessels enter the cartilage from the subchondral marrow spaces which invade from below upward. Thus the cartilage becomes more and more compromised, is changed first to fibrous cartilage, or immediately to connective tissue. The vascular connective tissue of the upper and lower surfaces of the joint then unite, or a papilla grows directly into the opposing joint surface. Thus the latter become adherent, partially or totally, and the joint is fixed in its position (ankylosis fibrosa), as the capsule and the periarticular tissues are thickened and sclerosed. If the fibrous covering of the joint surfaces undergoes ossification, the condition is known as ankylosis ossea. This may lead to an internal cementing of the bones constituting the joint which Ziegler calls arthritis ankylopoetica.

Another name frequently used is chronic progressive polyarthritis, or arthritis atrophicans. Exceptionally, marginal outgrowths of the joint surfaces, usually of localized extent, are added to the growths of the synovial membrane. This is actually a combination with arthritis deformans, and occasionally the transition to this disease is more obvious, inasmuch as the growth processes in the cartilage and bones become more pronounced, and there is a progressive disappearance of the joint ends as in arthritis deformans. In such individuals, one joint may show one type and another the other type of change.

Arthritis chronica adhesiva may be (*a*) the end stage of various acute and chronic joint inflammations, usually of destructive nature, particularly tuberculous; (*b*) it may be more independent inasmuch as it is the most frequent anatomical basis of chronic rheumatic polyarticular arthritis (the so-called arthritis pauperum, named in contrast to arthritis uratica, gout, a disease of the rich). It may develop from an acute polyarticular (infectious) joint rheumatism or it may be chronic from the beginning; in either case, it runs a progressive incurable course. It develops most frequently in smaller joints such as those of the toes and fingers, with muscle atrophy, displacements, subluxation of the ends of the joints, pseudo-contractions of the tendons (particularly the flexor), etc., and produces more or less deformities, as in fig. 649. Occasionally, however, the shoulder and the knee joints are involved; indeed, all of the joints have been known to be involved by the same disease. Much is obscure in the etiology; rheumatic injuries, such as exposure to cold, wet, damp living quarters, etc., have been blamed. The disease is much more frequent in women of middle age, but occasionally appears in younger women, as well as in those of advanced years, although the latter is more rare. That which Curschmann calls polyarthritis chronica deformans is probably the same condition. He emphasizes especially its beginning in the ligaments and in capsules; between these parts and the soft parts there is a doughy swelling and infiltration.

An ankylosing arthritis may also result from inactivity of a joint. If joint surfaces are placed completely at rest, *e.g.*, in paralyses, or luxations, or contractures, the cartilage begins to shred where the pressure is removed; it is covered by synovial membrane, and adhesions develop between the opposing joint parts. Such a joint, immobilized for a long time, can be moved only by force, tearing the adhesions, and often the shortened joint ligaments. [For arthritis, see Pemberton and coworkers, J. A. M. A. 75: 1759: 1920, Am. J. Med. Sci. 161: 517: 1921, and 166: 833: 1923, J. A. M. A. 85: 1793: 1925.—*Translator*.]

Appendix. The Neuropathic Arthropathias.—These joint changes, the most important of which occur in tabes dorsalis and syringomyelia, are believed to be due to nutritional disturbances produced by the disease in the nervous system. But others doubt this (Gowers, see Jensen, lit.), because they doubt the very existence of trophic nerves and centers; but ordinary sensory and motor nerves are always injured in these arthropathias. The changes may appear as arthritis ulcerosa sicca, or may resemble arthritis deformans, so that many authors believe tabetic arthropathia is really an arthritis deformans (Budinger); in fact Barth hypothecates a nervous lesion in arthritis deformans just as does Senator; in many cases, however, certain anatomical peculiarities are manifested. In tabes, it is usually the lower extremities, in syringomyelia usually the upper extremities that are involved (Zesas). In tabes the joint most frequently involved is the knee, either uni- or bilaterally, but others have been reported, such as the shoulder, the hip, etc., (data by Schlesinger). Attempts have been made to separate arthropathie tabetique from arthritis deformans. The sudden appearance, the transudation of fluid, the marked swelling, even of the neighborhood, the rapid, entirely painless course, the predominance of destructive changes in the ends of the joint, in contrast to new formation, differentiate tabetic (and also syringomyelic), arthropathias from the others. As a matter of fact, when the anatomical types of atrophic forms (*a*) are examined, as illustrated by Charcot, Oppenheim, Budinger and others,—a thigh without head, neck and trochanter; a tibia, the upper third of which disappeared to an anterior leaf; a humerus, the entire upper third of which was lacking; an otherwise unchanged socket with a colossal defect in its base;—then every similarity to arthritis deformans disappears. Remember the fact that particularly in tabes, the analgesia, the diminution in the space sense, the ataxia, the traumata, etc., naturally increase the intensity of the arthritis. Since destructive changes occur so very quickly in the ends of the joint, and relax the capsules and ligaments, it is obvious, that severe deformities, such as luxations or subluxations may occur in a very short time. But the atrophic form is not the only kind of these arthropathias. Perhaps more frequently we meet an hypertrophic form (*b*), in which bone disappearance is accompanied by vigorous growth so that mild cases allow practically no differentiation from arthritis deformans. The extreme cases of the hypertrophic form, however, have peculiarities of their own produced by the contrast of marked disappearance and enormous growth, both more marked than ever occur in arthritis deformans; in fact, this combination is unusual in ordinary arthritis deformans. The bony ends of the joints may spread and become misshapen; bony and cartilaginous outgrowths and flat hyperostoses appear (for example, in the circumference of a socket), as well as free, often large, joint mice, and,—particularly impor-

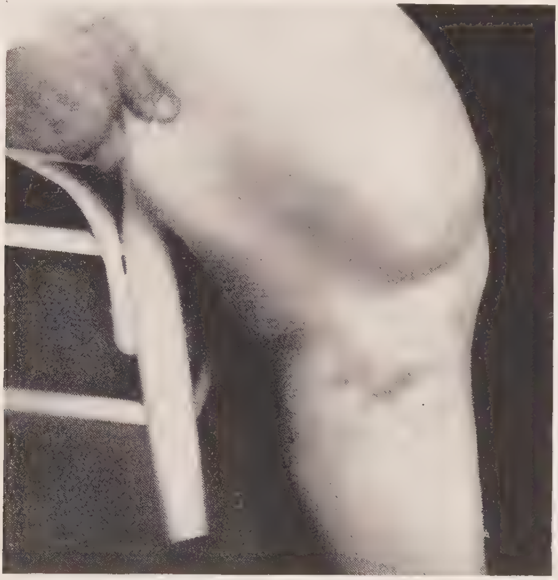


Fig. 650.—Charcot's joint in a patient 50 years old. Present for several years. Non-painful, non-tender. The joint was unable to bear any weight, but sagged in various directions on any attempt to stand on the leg. L. H.

tant,—enormous peri- and paraarticular bone growths, in the form of thick, plump shells, accompanied by ossification of neighboring soft parts and the formation of exostoses, which may penetrate the muscles like long lead pencils (as in myositis ossificans). The peculiarity of such cases is further emphasized, according to our opinion, disregarding the course of the disease (sudden beginning, rapid painless development), by demonstrating that other joints are free of arthritis deformans. The thickened bones, as well as the distinct bony overgrowths, are rarefied and porotic, but this may occur in tabes without arthropathia, and even lead to spontaneous fractures (see p. 1070). Concerning diseases of the vertebral column with rapid thickening, periarticular ossification, and atrophy of the bony tissue, followed by kyphoscoliosis, see Frank (lit.).

See also lit. by Levy and Ludloff, Oehlecker, Matsuoka, Kawamura, Hildebrand. For arthropathias in psoriasis, see Waelsch (lit.); in leprosy, see p. 1262.

Gout, Arthritis Uratica s. Urica. This disease seldom appears before the fortieth year, is usually hereditary; its actual cause is an obscure constitutional anomaly (it is also called the uric acid diathesis); it is characterized by the deposit of brittle, chalky white masses composed mostly of crystalline uric acid salts, chiefly sodium biurate, in the joints and their immediate neighborhoods. The cartilage is chosen primarily (p. 1231). The predominance of the male sex is quite striking. (Arthritis uratica is called erroneously, "the gout of the rich," and is believed to be due to high living, in contrast to arthritis pauperum, p. 1249.) A second predisposing cause in addition to heredity is exogenous: chronic lead poisoning, in painters, etc., which leads to secondary uric acid retention (secondary gout), because it damages the uric acid secreting parts of the universally diseased kidney (Brucksch and Schittenhelm, Thannhauser); alcoholism, the administration of too much purin. Uric acid, trioxypurin, is the end product of the action of enzymes on purin bases, the chief source of which are nuclear substances. (For review of gout, see Umber, Munk, Brucksch; see also M. B. Schmidt, Gudzent.)

According to Ebstein, in general, a circumscribed necrosis of the tissue is a preliminary necessity for the deposit of the urates; this necrosis is said to be due to the presence of dissolved uric acid salts. According to Garrod, the investigations of Riehl, Aschoff, Freudweiler and His, F. Rosenbach, etc., the primary condition, however, is the deposit of the urates, and these lead to an inflammation accompanied by necrosis; but, on the other hand, sodium biurate in crystalline form may be found in anatomically intact tissues, and act merely as a foreign body. We can probably state that necroses do not occur without urate deposits. Indeed, Krause doubts the occurrence of "tissue" necroses; they appear rather after complete solution of the crystals which leave behind a finely granular, entirely structureless mass, which Benneke, who has recently adopted the theory of Ebstein, believes is due to an intensive necrosis of the tissue. He believes that the chief causes of these necroses are embedded masses and inclusions of the crystals, even though occasionally actual bits of tissue are pulled apart or enclosed by the crystals and contained in the masses. According to Munk, precipitation of the uric acid, *i.e.*, the formation of tophi, which contain an albuminous stroma, occurs like the precipitation of urinary and gall stones, *i.e.*, colloids are as important as the uric acid.

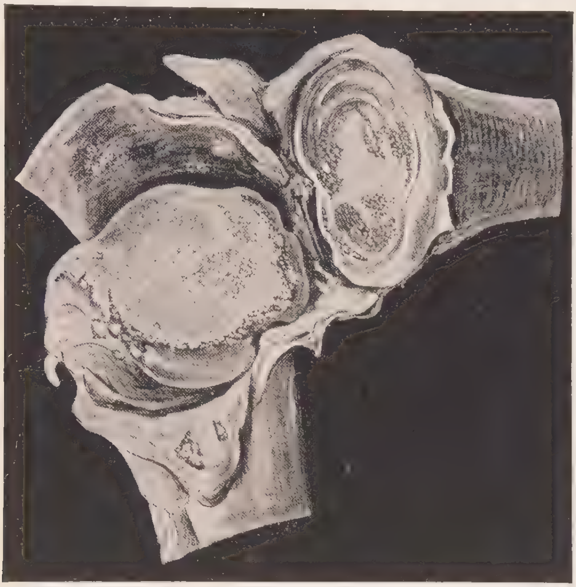


FIG. 651.—Opened gouty joint. Metatarso-phalangeal joint of r. large toe in uric acid arthritis. Diffuse white incrustations in joint; on marginal areas, extensive formation of bone and cartilage; joint capsule also incrusted; man 42 years old with gouty contracted kidney, cardiac hypertrophy (weight of heart, 705 gms.); necroses and scars in myocardium; parietal thrombi in r. heart, infarct in lung; ⅞ nat. size.

In the experiments of Freudweiler and His, quite large amounts of urates were absorbed from the skin, the peritoneum and the joints by leucocytic granulation tissue with peculiar spindle cells and giant cells. Such resorptive processes with the appearance of giant cells (urophages), have been described by Riehl around tophi, and also by von Rindfleisch. Aschoff and others saw similar cells in the uric acid deposits of the kidneys and the cartilage.

Deposits may also occur in the bones and the synovial membranes. But the chief sites are the capsules and ligaments of the joints, the periosteum, the surrounding parts, such as tendons and bursae, and the subcutaneous and intramuscular connective tissues (gouty nodules, tophi arthritici). In most cases, but one joint is involved at first, usually the metatarsophalangeal joint of one large toe (podagra), but occasionally other joints of the hands or fingers (cheiragra) or the knees (gonagra) are the seat of the deposits.

As a rule, the joint quickly swells and gives much pain. The neighborhood is reddened, and the soft parts, particularly the skin, are infiltrated with serum; in hours or days, everything returns to status quo. In spite of frequent recurrence of attacks, the joints may return to normal, but internally they appear as though covered with cloudy white spots and flat deposits; severer degrees make the joints appear as though smeared with plaster of Paris (actually the deposits are in the tissues), but this is often the only change. (In asthenic gout, the attacks decrease in intensity and finally cease entirely.) In some cases, the joint does undergo changes because of the shredding, ulceration, or growth of the cartilage, and thickening of the synovial membranes of the fibrous joint capsule; occasionally a fibrous or even a bony adhesion between the ends of the joints occurs as in arthritis chronica adhesiva. In severe cases, the urates are collected around the joint in the form of thick, chalky nodules (tophi arthritici, gouty nodules), which naturally change the contours of the parts. Not rarely, necrotic softening appears around the deposits, or even a phlegmon; softening cavities are filled with pus and urates may perforate broadly, or through fistulae through the skin; fissures and ulcers are common, from which urates and necrotic tissue masses are emptied. In other cases, the reaction of the surrounding tissue produces a more or less tough fibrous capsule around the focus. The hands may become so deformed and stiff that the fingers lose their usefulness (Pfeiffer). A condition often falsely called "gouty fingers," and mistaken for gout, are Heberden's nodes, a disease which has nothing to do with gout, but in which pea shaped bony thickenings are deposited, first in the distal, phalangeal joints of the fingers. According to Munk, it is clinically and anatomically different, but, according to others, similar to arthritis deformans or related to it (Wick, Heckmann, Jacobsohn); according to Pineles, they are produced by osteophytes. They occur usually after the fortieth year of life, more frequently in women at the time of the menopause or immediately before, and are said to have some relationship to the involution changes of the genitals at this time. According to Marie and Leri, Heberden's nodes in old people occur coincidently with thickenings of the bones of the hands and middle finger; elongated and broad protuberances appear on the upper and outer parts of the back of the hand; these changes are said to be identical with those of chronic rheumatism. In addition to those described above, urates may be deposited in the kidneys, and situations of the skin and the subcutaneous tissue, with preference for the bursae of the olecranon, in the cartilage and the subcutaneous tissue (according to His in this alone), in the pinna of the ear, where they produce pea-sized nodules, often in large numbers, surrounded by dilated veins, more rarely in the eye-lids, the cartilages of the nose, or even in the cornea. The pericardium, pleura, meninges, both cerebral and spinal, the prepatellar bursae, the bursae of the olecranon, more rarely the testes (Tower), may also be the seats of deposit. Atypical gout, without actual gouty attacks, but with deposits particularly in the prepatellar bursae, and in the bursae of the olecranon, has been described by Goldscheider. Individuals with the uric acid diathesis often suffer from lithiasis (formation of uric acid stones), and have shrunken kidneys; but a gouty joint may persist for many years without the kidneys necessarily being anatomically changed. According to newer investigations, the uric acid content (Gudzent) of the blood (uricemia), is increased, even though not constantly, in both gout and lithiasis, but not in the urine (Chauffard and others). Gouty individuals occasionally suffer from lipomatosis and diabetes. (For attempts to treat gout with cartilage extracts, see Heilner.)

The Changes in the Joints Produced by Tuberculosis and Syphilis.

Tuberculous Joints.—There may be differentiated: (*a*) pure tuberculosis of the joints, which consists of isolated nodules following the invasion of tubercle bacilli, while the synovial membrane is otherwise unchanged, *i.e.*, shows no recognizable symptoms of inflammation; this occurs occasionally in general miliary tuberculosis; (*b*) those tuberculous joint inflammations which progress with inflammatory changes, particularly overgrowth of the synovial membrane. These belong to the most frequent chronic arthritides. According to the point of origin there are differentiated: (1) primary tuberculosis of a bone (one caseous focus), rarely of a tendon sheath, extension secondarily into a joint. This primary osteal form comes from a tuberculous focus, by way of the smaller lymphatic channels, or in continuo from a tuberculous focus in the bone which ruptures grossly into the joint, and in which sequestrae may appear which infect the synovial membrane (fig. A, p. 1126). This is the more frequent form and leads more quickly to extensive destruction. (According to Konig, for example, the condition appears in the knee joint in two-thirds of the cases; Riedel, for the hip joint, says 84% are from primary osteal foci, 70% with the formation of sequestrae, for the ankle-joint 64% primary osteal, 36% primary synovial disease; Konig, for the elbow joint, 71% synovial. In the joints of the hand the primary synovial form is probably more frequent.)

(2) Primary synovitis tuberculosa (granulosa and fungosa), or the primary synovial form of tuberculous joint inflammation, is characterized

by more or less distinct tubercles, or by diffuse tuberculous overgrowths, while the synovial membrane reacts with a chronic inflammation. An exudate also appears in the joint cavity. The synovial membrane becomes hyperemic, swells, grows, and to a greater or less extent becomes a soft, spongy, moist, pale gray red, granulation tissue. Gray, to gray white, or yellow, (caseous) foci or spots are microscopically characteristic tubercles with epithelioid and giant cells, and caseation (Koester). These are fungoid granulation or tuberculous granulation growths. The tuberculous caseous inflammation is called fungoid or joint fungus.

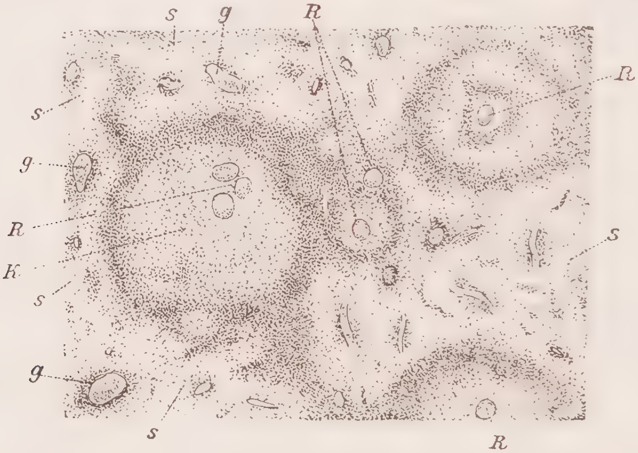


FIG. 652.—From a tuberculous inflammation of a joint. Granulation tissue with tubercles in the proliferating, cellular and vascular synovial membrane (s). R, giant cells; K, caseation in tubercles; g, blood vessels in the proliferating synovial membrane, frequently surrounded by larger groups of cells. (Low power.)

The number of tubercle bacilli is strikingly small, and they can be found in joint tuberculosis only after very careful and long continued search. But this is only similar to tuberculosis of the bones and many forms of tuberculosis of the lymph nodes.

The relation of the growth of the synovial membrane (its basic stroma), to tuberculous deposits varies considerably; in many cases, the membrane is fairly tough, poor in cells, infiltrated by innumerable distinct tubercles, and changed to a thick, somewhat transparent, pale gray red, granular structure, which is easily pulled off from the capsule (so-called granular form). In other cases the soft granulating membranes show cloudy yellow, caseous, poorly outlined, masses of larger extent. Distinct microscopic nodules are very scarce. Those forms in which the fungoid granulations undergo quick caseation, lead very rapidly to ulcerative destruction (tuberculous joint caries), and occur most frequently in the osteal form of joint tuberculosis. Focally, the overgrowth of the synovial membrane takes on a form similar to that in non-specific chronic arthritides. Papillary outgrowths or veil-like membranes similar to edematous connective tissue push their way in between the overlying cartilaginous surfaces.

But the membrane is also covered with an exudate, which may be serous (hydrops tuberculosus), sero-fibrinous, sero-purulent, fibrino-purulent, or purely suppurative (empyema articuli tuberculosum), fibrino-purulent or purulent, when there are many tuberculous granulations undergoing rapid destruction.

In other cases, a spongy tissue appears without suppuration (pure fungus form).

Occasionally also, free bodies appear in enormous numbers as the so-called corpora oryzoidea, or rice bodies, mellon seed-like yellow white, elastic, lamellated masses composed of fibrinoid bands and layers. Schuchardt believes they originate from loose particles of the hyalin synovial connective tissue, but Goldmann believes they are fibrinoid degenerated granulation tissue, which has been lifted from the surface of the tuberculous membrane. He also believes this granulation tissue is a prestage of both the fungoid and fibrinoid degeneration which produces these rice bodies. They usually float in a clear serous exudate. Bacilli have been found in the rice bodies both by staining methods and by animal inoculation (peritoneal cavity, Garre). The condition is so typical that it has been called the "rice body disease," and is often found in the tendon sheaths and bursae, as a clinically benign form of tuberculosis (Garre, Goldmann). Others believe rice bodies are the fibrin of exudates (Konig, Riese), and it is quite probable that fibrin masses may occasionally assume their appearance.

The changes in the joint cartilage are varied. Tuberculous granulation tissue enters the cartilage from above downward, from below upward (from the bones), or upon it from the overgrown synovial membrane, or from the marrow tissue; it infiltrates the cartilage and shreds it, ofttimes from both below and above. The situations of the cartilage on which pressure is exerted, are usually the first to undergo complete disappearance.

If the surface of the cartilage is covered by the granulations, it may be invaded from above downward, whereupon the ground substance becomes soft or swollen, and the cartilage cells undergo growth; later the capsules of the cells are opened and then filled by connective tissue, so that the cells soon undergo destruction. Thus the cartilage is focally destroyed, ulcerated, defective, or traversed by many passages containing occasional blood vessels. Not rarely, a simple overgrown synovial membrane is laid down on the cartilage similar to a tender gelatinous edematous connective tissue, and soon the cartilage becomes a granulating or myxomatous connective tissue.

But if the granulations extend down to that part of the cartilage lying near to the bone, or into the subchondral layers of the marrow, or if the granulation focus is originally present in the subchondral tissue, the entire cartilage is peeled off, or completely lifted off so that it lies free between the joint surfaces (particularly in the hip), or is perhaps ulcerated from below and finally perforated like a sieve. The cartilage cells respond by slight degrees of growth. Then leucocytes enter the spaces of the cartilage and may even reach the lacunae (Orth, Heile). Meanwhile granulations protrude from the perforations like tongues, or grow like fungi from the surface. Similarly, but less intensively, the subchondral marrow takes part in the overgrowth without being necessarily tuberculous. It is usually richly vascular, gelatinous or lymphoid, and enters the cartilage like marrow spaces. Giant cells may become chondroclasts (Seggel).

This non-tuberculous overgrowth of the marrow tissue produces, or accompanies an osteoporosis in the surrounding parts of the bones.

Resorptive processes are noted in the bony trabeculae, particularly many lacunae with osteoclasts. Smaller bones, for example, those of the ankle, may become so porous by overgrowth of their marrow, that they can easily be perforated by a probe. On the other hand, osteoblasts also appear in considerable numbers and build new bone.

The parts of the bone laid bare by destruction of the cartilage, become carious, the more so the more the granulations tend to destruction, caseation, or suppuration. It is usually most marked in the primary osteal forms, particularly in the larger joints of the extremities (coxitis, p. 1259). This may soon lead to extensive destruction of the joint (arthrocace), to the accompaniment of vigorous suppuration.

As the changes progress within a joint, external observation reveals swelling of the entire joint region, in earlier stages produced chiefly by edema; in older stages the capsules, the ligaments, the intermuscular tissue, the neighboring tendon sheaths, the subcutaneous tissue, in fact, the entire neighborhood of the joints, are all thickened by a chronic hyperplastic inflammation. The structures around the joint thus are replaced by a tough, cicatricial, bacony connective tissue; it feels hard and appears white, waxy (glistening tumor albus). As the granulations grow, undergo caseation or suppuration, the whole becomes the so-called cold tuberculous abscess, with or without fistulous passages.

Very few tubercle bacilli can be found in these abscesses. The latter, as well as the fistulae, are lined with fungoid granulations; the fistulae occasionally communicate with the joint, but often rupture externally through the skin; growing like fungi from the opening, the granulations may exude much pus. In fact, the exudate within the joint cavity may be discharged externally through the fistulae which ramify between the muscles and fasciae in all directions (p. 1127). But suppuration, abscesses and fistulae are not constant in fungoid arthritides, for cases occur which lead to important destruction without suppuration (caries sicca).

Another condition in the immediate vicinity of a joint is periosteal overgrowth in the form of osteophytes, often very numerous and sclerotic, usually with stalactite or bizarre forms. Osteosclerosis is also produced as a result of the inflammation.

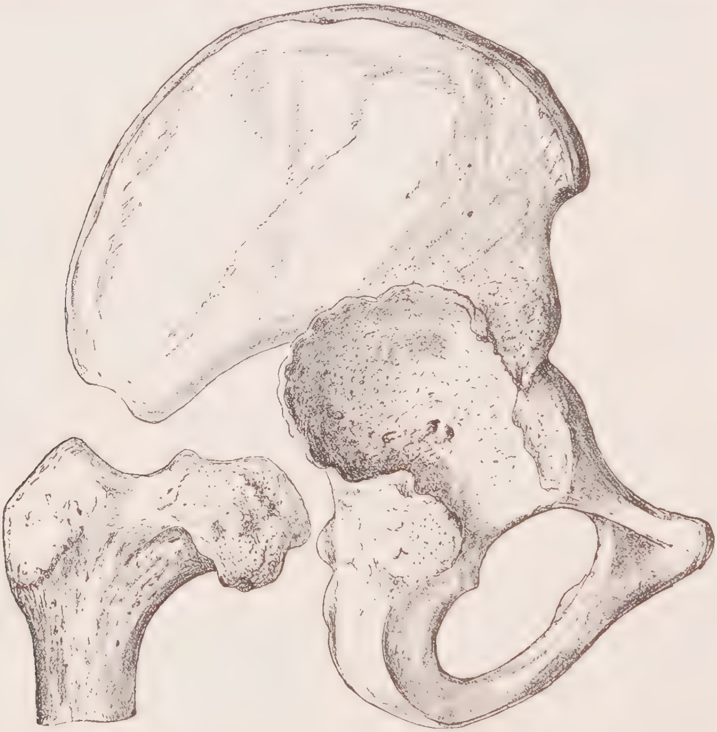
The further the destruction is spread, the more the joints become loose and assume false positions; pathological or spontaneous luxations, destructive luxations, or subluxations, are the best measure of the extent of the destructive process in the bones and ligaments, a fact of clinical importance (v. Volkmann). Finally, when all the ligamentous apparatus is loose, a flail joint results.

Situation.—The joints most frequently involved are the knee, the hip and the elbows, but the smaller joints are not spared.

In the knee, the predominant form is the fungoid and hyperplastic overgrowth; the knee becomes hard and spindle shaped, its greatest breadth lies in the region of the condyles, of the articular space. The male sex is more frequently attacked. In the elbow and shoulder joints a caries sicca is particularly frequent. The most marked destruction of the bones occurs, as a rule, in the hip joints (fig. 653). The capsule and the surrounding bony tissue may be destroyed over larger areas; the carious widening of the acetabulum and the displacement of the head of the femur to the sacrum, produce the so-called wandering of the acetabulum, and the so-called intraacetabular luxation of the head of the femur (figs. 653 and 654). This is not an actual luxation; the head is pulled up by the muscles into the pathologically dilated acetabulum which is often perforated. Tuberculous infection of the bordering peritoneum, as well as of the iliac and inguinal lymph nodes, is a frequent result. The extensive destruction of the head, the wandering of the acetabulum, the spontaneous luxation, the internal flexion and rotation, produce an important shortening and a false position of the leg which destroys its function.

Etiology.—Joint tuberculosis develops most frequently in children and youths. There is often a so-called hereditary taint. Traumata (falls, pushes, crushes) according to clinical experiences, play a role, and probably are a predisposing cause for the localization (according to Pietrzikowski, in about 20%). The animal experiments of F. Krause (injection of tubercle bacilli into the blood, crushing of a joint, localization of the bacteria in this joint), also gave grounds for believing that traumata help in the localization of tuberculosis. But Friedrich, who injected mildly virulent tubercle bacilli into the blood, saw no localization in the traumatized joints and bones. He expresses the opinion, however, (shared by Pietrzikowski, lit.), that traumata, particularly contusions and distortions, are capable of mobilizing an already existing latent tuberculosis. Tuberculous joint disease sometimes follows acute infectious diseases such as measles, scarlet fever, influenza.

Relationship to the Rest of the Body.– Joint tuberculosis may be the primary and only clinical manifestation of the disease; such cases naturally present the best therapeutic opportunities, and a general distribution of the infection may not occur, as it does in many cases. More frequently there are coincident other clinically manifested chronic tuberculous processes, such as the so-called scrofulous changes in children (p. 260), or pulmonary tuberculosis in adults. An infection of the regional lymph nodes is common; a chronic general infection is occasional; acute miliary tuberculosis or tuberculous meningitis also occur. It is important to consider that general miliary tuberculosis may follow operative procedures on tuberculous joints (v. Volkmann). Frequently, however, as in bone tuberculosis, no further infection of the organism takes place from the



FIGS. 653 and 654.—Tuberculous caries of r. hip joint. Large carious widening of the acetabulum (so-called acetabulum wandering upward or backward); from a phthisic 23 years old. Said to have followed a fall on hip during 7th year; ½ nat. size. Very marked carious destruction of head of femor, from same case.

tuberculous joint. Occasionally amyloidosis leads to death, particularly in the case with severe suppuration of long duration.

Healing.—In very early stages, ideal healing may take place with complete retention of function. (We cannot discuss in detail the events occurring in joint tuberculosis when treated with Bier's hyperemia, which has as its object the production of a cicatricial change of the tuberculous granulation tissue.) Many times the healing is merely a seeming one through encapsulation, and even after many years it appears anew. But under favorable circumstances, even severe cases heal, but always with prolonged disturbances of the function of the joint. Thus the movements of a hip joint are always more or less limited or entirely destroyed. Ankylosis by fibrous cicatricial union of the granulating parts, or by bony overgrowth (synostosis), is related to suppuration, or to the presence of a bone sequestrum. Unfortunately, the ankylosed joints often assume a deformed position, which is due, not in its least part, to shrinking of the capsule, and secondary (lipomatous or fibrous) atrophy of its muscles. Many joints such as the knee, elbows, hands, are usually fixed in flexion. The ankylosis of the hip is in flexion, usually with abduction and external rotation, though occasionally also with adduction (fig. 655). Marked inhibition of growth may occur in the limb belonging to a tuberculous joint, *e.g.*, the tibia after fungus genu, chiefly in youthful individuals; in such cases the ossifying epiphyseal line is destroyed. But occasionally, vice versa, the irritation of the line leads to an increased growth, *i.e.*, an elongation of the tibia (p. 1188).

Syphilitic Changes in Joints.—They are uncommon. An osteochondritis congenita leads to solution of the epiphyses and rupture into the joint. Congenital lues sometimes initiates exudative arthritides in the knees during the growth period (v. Hippel, Jordan); for more details see Bosse. Harttung observes that congenital, as well as syphilis acquired in early youth, lead to disease of the vertebral joints with subsequent deformity of the vertebral column. In the early periods of the lues of adults, *i.e.*, with the outbreak of the exanthem, acute serous transudations in joints may be accompanied by fever, particularly when in the large joints of the extremities, but occasionally also in the sterno-clavicular joints. In tertiary lues and in syphilis congenita tarda (Bergrath, lit.), there occur simple chronic hydrops, depending, according to Borchardt, upon the formation of miliary gummata in the synovial membrane, or larger gummatous overgrowths or their residues. Two groups of gummatous conditions may be recognized: (*a*) perisynovitis and consecutive synovitis gummosa (Jastrebow), a gummatous growth which spreads from the capsule and the periarticular connective tissue or from the periosteum into the joints; papillae of gummatous structure are developed. The gummatous masses invading the cartilage produce ulcerative defects, which may extend into the bone, and later heal smoothly or leave behind sharply outlined furrows in an otherwise entirely unchanged cartilage or bone; (*b*) the primary osteal form invades the cartilage and the soft parts of the joints secondarily, and usually produces more extensive disturbances. Suppuration and ankylosis have been known to result (Gangolphe, Fouquet, Zesas, lit.). See Bergrath (lit.) for syphilitic joint diseases in x-ray pictures. See also Wysocki, Guszmann, Reschke, and particularly Ashausen.

In a case briefly described by the author (65 year old woman, a syphilitic 15 years), the disease appeared in both knee joints in corresponding situations, at the anterior angles of the internal condyles of the femur; in the left knee joint there was an irregular, angular, deep, smooth, furrow about the size of a cherry, in the right knee there were gummatous masses invading the joint deeply into the bones and the cartilage, which produced the same angular boundary as on the left side. This case belongs to the form described under (*a*).

Differential diagnosis: (*a*) lues can be diagnosed with certainty only when gummata are found, particularly when they are multiple; the Wassermann reaction should be positive. (*b*) Tuberculosis. Swelling, pain, destruction, disturbances of function are greater than in (*a*) and (*c*). (*c*) Arthritis deformans: in addition to ulcers, which are not surrounded by unchanged cartilage and bone as in syphilis, there are overgrowth processes in the cartilage and bone. These defects are often surrounded by hypertrophic ridges.

Leprosy produces changes similar to arthritis deformans, or, in other cases, to the arthropathias of tabes and syringomyelia, namely, leprous feet; in the latter cases, the analgesia, anesthesia and muscle atrophy which are produced by the neuritis, relax the joint, and make its movements ataxic; they are combined with high degrees of bone atrophy (p. 1148), which explain the deformities without making it necessary to assume there are changes in the spinal cord, or in hypothetic trophic nerves. (Hj. Heiberg, Harbits.)

Tumors of the Joints.- Primary tumors are very rare, such as lipomas, angiomas, papillary angiofibromas, sarcomas, usually coming from the capsule (v. Ruediger, lit., H. Burckhardt, Hannenmuller, Lejars and Rubens-Duval, Reichel-Nauwerck, Zullig). (Comprehensive lit. to 1920 by Enderlen.) Lately, a number of joint chondromas have been described, and may be divided into the intraarticular and the joint capsule varieties (chondromatosis, Reichel, Riedel). Those coming from the synovial membrane (according to Rehn at the transition to the periosteum), clothe the entire joint (always an isolated hip, knee, elbow, shoulder, hand joint, etc., Kienbock), with innumerable nodules, and by pressure may extend into the capsule, ligaments, muscles, and the fat, and, as in the right knee joint described by Lexer, into the bones and cartilage. Causes: not inflammatory (as in the changes described on p. 1243), but probably from embryonal anlage (stray germinal cells?, failure in the differentiation of the mesenchyme, see Lexer; lit. by Eden, Troell, Kopp, Lotsch). The ganglia (see under tendon sheaths) and the hernia-like joint diverticulae are considered by Floderus to be arthromas (histioid joint tissue tumors).

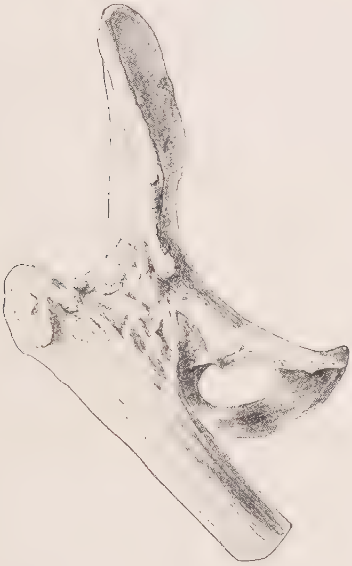


FIG. 655.

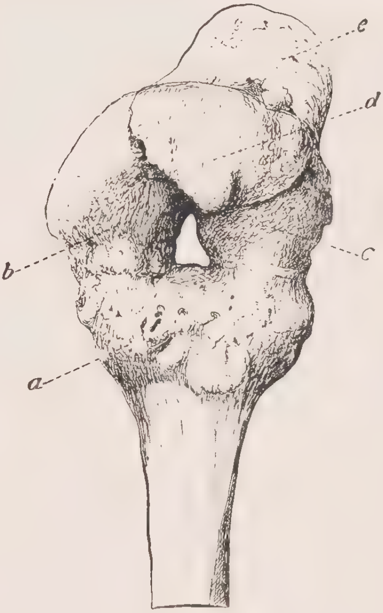


FIG. 656.

FIG. 655.—Bony ankylosis of r. hip joint; man 34; death due to chronic pulmonary tuberculosis; about ¼ nat. size.

FIG. 656.—Bony ankylosis of l. knee joint with synostosis of patella after purulent inflammation of joint following osteomyelitis of femur. Hyperostosis and sclerosis of femur (e); diameter of shaft, 5.5 cm.; of epiphysis, 9 cm.; a, tibia; b, ext. condyle; c, int. condyle; d. patella.

More details under ganglia. Secondarily, a primary bone tumor or a metastatic tumor in a bone may invade a joint.

Appendix.—The following changes can be but briefly described. For more details, consult works in special surgery.

Ankylosis.—Formerly, ankylosis meant an angular position, but now it means complete absence of movements, *i.e.*, fixation of a joint in a certain position produced by disease of the joint itself. The term intracapsular ankylosis is also used. The bones belonging to a joint are fixed with respect to each other. If the fixation occurs because of thickening of the capsule, the condition is known as capsule ankylosis. If produced by changes in the neighborhood of the joint, such as cicatricial shortening of the soft parts, contractures of ligaments, muscles, fascias, etc., the condition is spoken of as extracapsular ankylosis. A particular form of the latter is the fracture ankylosis, a more or less complete fixation of a joint, produced by clothes pin-like bony bridges coming from the outside of the joint.

In ankylosis vera, the bones are fixed totally; in incompleta or spuria, they are still somewhat movable. The union of joint ends may occur through fibrous, rarely cartilaginous, or through bony tissue. The cartilage may disappear, since it is necessary to have certain physiological stimuli for its retention (pressure and movement), (Roux). Ankylosis fibrosa, cartilaginea, ossea, are the terms used when the bony ends of a joint are directly united by one or the other of these three tissues. If a part of the joint cartilage remains, and consists almost entirely of a fibrous adhesion, the term ankylosis fibrosa intercartilaginea may be used. Immobilized joints, even though not diseased, may become ankylosed, though rarely; according to Moll, connective tissue formation takes place at situations where the ends of the bones are not in contact; where contact is assured the cartilage remains normal. Ankylosis ossea develops after destruction of the cartilage, *e.g.*, after suppurative arthritis (fig. 656). The surfaces of the bone in such an ulcerated joint naturally behave like the ends of fractures. The surfaces may disappear in bony union and trabeculae are produced directly from growing germinal tissue, or there may be an intermediation of a cartilaginous fibrous adhesion in which bone is secondarily deposited. The growing periosteum and the parosteal tissue may also produce ossified union of the ends of a joint.

Changes in the Architecture in Ankylosis.—When an ankylosis develops in a younger individual whose period of growth is not over, new static demands are made during this growth and the architecture responds correspondingly (the laws of transformation of Wolff); this is usually accomplished by the least possible amount of bone to serve the purpose. But even when the growth of an ankylosed bone has ceased, changes in the statics lead to a similar rearrangement of the architecture, *i.e.*, to a functional adaptation (Roux); but not by moving the rigid parts, rather by absorption of trabeculae that are superfluous, and deposit of new bone where the changed pressure and pull stresses are laid. Thus in an angular ankylosis, the bony parts on the concave side become denser (the hypertrophy of activity, Roux), those on the convex side become more porous.

Scoliosis, Kyphosis, Lordosis.—These terms define bowing of the vertebral column laterally, posteriorly and anteriorly. Physiological scoliosis is a mild bending of the thoracic vertebral column (third to fifth vertebrae) to the right. This bowing increases under pathological conditions such as uneven strain of the vertebral bodies in poor postures, *e.g.*, during writing, piano playing (particularly in girls), etc., and following softening of the vertebral bodies in malacia (rickets, osteomalacia, ostitis deformans), senile and inactivity atrophies or trophic disturbances (for example, hydromyelia, etc.), in habitual overuse of one side of a body, or in "constitutional weakness" of the supporting apparatus of the vertebral column (Schlesinger); thus the dorsal part becomes convex to the right, the lumbar part, to the corresponding opposite direction becomes compensatorially convex to the left, so that the consecutive crookedness may be more marked than the primary condition. The kyphosis is compensated by the lordosis, whereby the longer limb of the kyphosis takes up the compensation as far as it is not divided between both. The vertebral bodies turn on their axes so that they are turned toward the convexity of the bowing; in high degrees of bowing their forms undergo change until they become wedge-shaped; the bowing becomes fixed, is no longer mobile, and cannot be straightened. Severer degrees of scoliosis are usually accompanied by kyphosis (kyphoscoliosis).

For scoliosis following congenital anomalies of the vertebral column, see Naegeli. Insufficientia vertebrae (Schanz), a constitutional weakness of the vertebral column and its ligamentous apparatus as occurring in asthenics (p. 458), is discussed by Payr.

The aorta follows the crookedness, and the trachea in part; the esophagus insofar as it is not abnormally fixed, passes under the bifurcation, away from the vertebral column and courses over the deformity like a string over a bow (v. Hacker, Jawin). Even in marked kyphosis, the spinal cord is not compromised, as a rule; synostoses partly fortify the compromised vertebral joints. See H. Virchow, concerning the relationship of the musculature,—shortening, failure of useful adaptation, connective tissue changes, and fatty degeneration.

Kyphoscoliosis of the thorax (more frequently right convex), is serious for the organs of the chest cavity. As fig. 657 shows, the thorax is so misplaced, that the convex half of the thorax is diminished in all its dimensions; the ribs turn sharply posteriorly, are bent angularly (chest deformity due to scoliosis), and may finally touch the vertebral column. This compresses the corresponding lung which is forced forward from the narrow posterior part of the thorax into the equally narrow anterior part. The concave side, on the other hand, is increased in its lateral diameter, the ribs describe a large arc, are stretched, the angles of the ribs become flatter and flatter (fig. 657), but the direct, and particularly the longitudinal diameters, are smaller, the latter because the ribs are pushed over one another even to the extent of like the shingles on a roof. This space reducing compression of the lung is increased by displacement of the abdominal organs and the high position of the diaphragm; it consequently develops serious changes in contour as it becomes fitted into the crooked thorax, with atelectasis and partial destruction (Bertsch), while, the other lung must fill a dilated space, and thus becomes emphysematous.

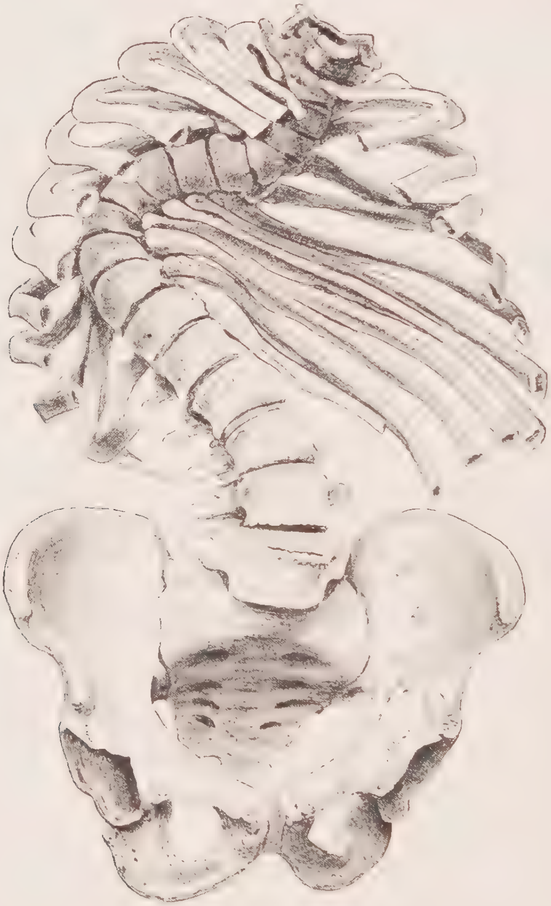


FIG. 657.—Kypho-scoliosis of spine of man 58 years old.

The increased resistance to the circulation produces stasis in the lungs as well as dilatation and hypertrophy of the right heart (E. Meyer, lit.). Thus the weight of the heart is always increased (up to 550 gms.). Failure of compensation which develops gradually or perhaps even suddenly following an increase of blood pressure during coitus, defecation, anger, etc., is the most frequent cause of death in those with severe kyphoscoliosis. (Concerning the changed situs of the thoracic organs, see also H. Virchow.) The organs of the abdominal cavity also suffer circulatory disturbances (stasis), changes in contour (transverse furrows of the liver), and often extraordinary displacement (see illus. by May, Ponfick).

Even the base of the skull may be bowed outwards by a scoliosis, (Froriep).

For more details concerning the various shapes of the thorax according to the situation of the kyphosis and its combination with scoliosis and lordosis, see Riedinger, Schulthess, Becher, Strasser.

Kyphoscoliosis also changes the contour of the pelvis which becomes oblique, the sacrum turned to the one or the other side, and the ala, on this side, shortened; the symphysis is likewise displaced—milder degrees are shown in illust. 657 (Breus and Kolisko).

Concerning rotation and torsion of the vertebral column as a reaction to displacement, see the interesting experiments of Sellheim.

In the so-called traumatic spondylitis (Kummell, Henle), and its resultant painful scoliosis, there is an ankylosing spondylitis due to a sprain or a compression fracture (see, for example, Eug. Fraenkel, Payr).

Concerning Pott's kyphosis in caries tuberculosa, see p. 1130. Lordosis, most frequently of the lumbar vertebral column, occurs sometimes as a compensation of an upper kyphosis, or from rickets, or from luxation of the head of the femur and its corresponding deformity of the pelvis, or from fixation of the hip joint in coxitis, when the tilt of the pelvis is increased; it also occurs in atrophy of the muscles.

According to Schulthess, static scoliosis develops from simple shortening of one leg following disturbances in growth, diseases of the joints of the foot, the ankle, the knee, (ankyloses, contractures), the hip (luxations, coxa vara, ankyloses, contractures in abduction or adduction), diseases and malformations of the diaphyses, and finally, elongation of one extremity (p. 1188). Concerning the method of examination, see Doerr.

Luxations of the Joints.—There are differentiated: (*a*) luxations, the parts of the joints are completely separated from each other, the capsule is torn; (*b*) subluxations, a prolonged displacement of the ends of the joints, without complete separation of the surfaces. The capsule need not be torn.

Distortion is a forceful momentary stretching of a joint (luxatio sponte reposita). The capsule and ligaments may be torn. Habitual luxations are recurring dislocations depending upon abnormal elasticity or tears of the capsule, or upon too little scar in a capsule previosly torn. Complicated luxations are those coincident with injuries of the bone or the skin.

There may be further differentiated: traumatic, spontaneous, congenital luxations.

Traumatic Luxations.—The capsule and ligaments are torn. The head of the joint protsudes or escapes through a tear in the capsule which is often slit-like in shape. If it is not soon replaced and the member brought to its normal position, it becomes a chronic luxation. The tear in the capsule may adhere. The muscles, deprived of their function, undergo atrophy. Around the head of a bone permanently dislocated, a nearthrosis may develop, *i.e.*, a sort of new, often quite sufficient, joint (Martini). Thus the luxated head of the femur pressing upon the ileum, assuming it remains movable, may bore its way into the bony structure which disappears by pressure atrophy. In other cases, the periosteum builds a wall of new bone, while the movable head becomes thickened by ostitis ossificans. Thus the head may be fitted into a new socket, and occasionally acquires a covering of cartilage. In traumatic luxatio centralis femoris, the head of the femur passes through the floor of the acetabulum. This is also called central dislocation of the hip joint. This form occurs as a pathological, or spontaneous central luxation in osteomyelitis, tuberculous destructive new growths, more rarely in echinococcus disease of the hip region (Henschen).

In still other cases, the luxated part becomes tightly adherent by fibrous or bony ankylosis to the surrounding bones and soft parts. If the luxated part escapes between soft parts, or externally, it may undergo atrophy. Occasionally a change occurs as in arthritis ulcerosa sicca. An empty joint cavity, *e.g.*, the acetabulum, or a free joint end becomes covered with connective tissue; the cartilage is shredded and changed to fibrous tissue. The socket is flattened, partly through atrophy of the old parts, partly through a filling out with new bone and connective tissue.

Spontaneous, pathological or inflammatory luxations occur from stretching of the ligaments, *e.g.*, in hydarthros (distension luxation), or from ulcerative changes in the joints (destruction luxation), the most important of which are due to tuberculosis. They are seen chiefly in the hip and knee joints. Subluxations are common in tumor albus of the knee (p. 1258). Consult coxitis tuberculosa (p. 1259). Paralytic luxations of the shoulder may follow paralysis of the shoulder muscles, *e.g.*, from acute anterior poliomyelitis; flail joints, descent of the arm, are the results since the muscle apparatus is the most important fixation material.

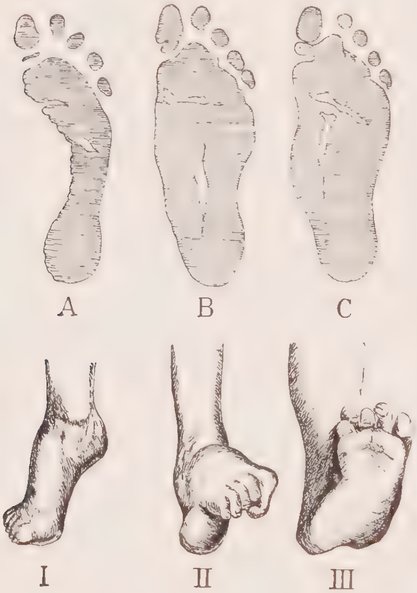
In **spondylolisthesis,** the lumbar vertebral column sinks into the pelvis because of displacement of the fifth lumbar vertebra. It is merely the body of this vertebra which slips, while its lower joint surfaces retain their contact with the upper processes of the first sacral vertebra, and the spinous process with its arches remains in its proper position. The slipping, which therefore is only of the vertebral body, is possible only from elongation of the interarticular portion of the fifth lumbar vertebra, and occurs with or without fracture; if without, it is thought that developmental anomalies such as syndesmoses, defects of ossification of the lumbo-sacral joint or of the arch of the fifth vertebra are predisposing causes, while the increased pressure of the trunk in perpendicular posture of the body, is the immediate cause. Pressure and rubbing may lead to disappearance of the intervertebral discs and to a synostosis between the vertebral surfaces. Narrowing of the conjugate diameters, lifting up of the entrance into the pelvis, following a shift of the heavy part of the trunk anteriorly, etc., are the results (lit. in appendix).

The Otto-Chrobak's Pelvis.—A coxarthrolisthesis-pelvis (pelvis Chrobak), first observed by Otto, and described by Eppinger as a narrowing of the pelvis, is produced by a protrusion of the cup of the acetabulum into the pelvis (protrusion of the floor of the acetabulum, intrapelvic protrusion). The cartilage of the socket becomes soft, elastic, and the growing femur head pushes it inward. According to Kuliga, however, similar changes may be caused by arthritis deformans. The author saw an outspoken case in a tabetic arthropathic, (48 year old man); the left acetabulum, surrounded by ossifying ridges, extended into the pelvis to a depth of 9 centimeters. This case has been analyzed by Breus; it was a protrusion of the acetabulum following trauma which fractured the acetabulum (and the pelvis generally), and thus differs from typical Otto's acetabulum; it is better not to consider that tabes caused the Otto's disease in this complicated case. Also the case of Chiari which occurred in a tabetic, does not positively prove that an Otto's protrusion may come from an arthropathia tabidorum (see Breus). According to Schlagenhaufer, it is spontaneous healing of a probable gonorrheal coxarthritis; Henschen, on the other hand, believes in a varied etiology, among other things, also tabes. But the investigations of Breus and Kolisko have probably shown that typical Otto's disease is due to a gonorrheal arthritis, although this does not exclude the possibility that other intrapelvic protrusions cannot have other etiologies (see Chiari and Valentin-Muller).

Congenital luxations are particularly frequent in the hip joint, and the knee. They are due partly to hypoplasia of the tissues of the joints depending on developmental inhibitions from early time; the acetabulum is sometimes so small that the head of the femur, even though smaller than normal, cannot fit in; other cases are acquired spontaneous luxations in later fetal times; abnormal positions of the lower extremities gradually push the head out of the acetabulum. Other luxations are traumatic during birth (lit. Joachimsthal).

According to Lorenz, the so-called congenital luxation of the hip is, as a rule, an acquired static deformity, but the predisposition to luxation is congenital in the form of a growth hindrance of the bones of the entire leg, the corresponding half of the pelvis and the acetabulum. Concerning rare congenital hip joint luxations of inflammatory origin, see Ranzel, lit.

Other Abnormal Positions of the Joints.—The chief forms of these conditions which depend both on developmental disturbances and thus are present at birth, but which also develop in previously normal joints are: pes varus, club foot, the soles turned internally (supination), the external edge of the foot pointing downward; pes varo-equinus, the foot is coincidently in plantar flexion; pes valgus, s. planus, flat feet, the soles externally (pronation), internal edge of the foot turned downward; pes calcaneo-valgus, flat foot in dorsal flexion (fig. III); pes equinus, horse's foot, pointed foot, sole pointed backward, the toes crooked, so that the foot (fig. I) on standing touches the ground with its toes and the anterior ends of the metatarsal bones; pes calcaneus, talipes calcaneus, directed downward, point of the foot directed upward (dorsal flexion, see fig. II).



FIGS. 658–661.

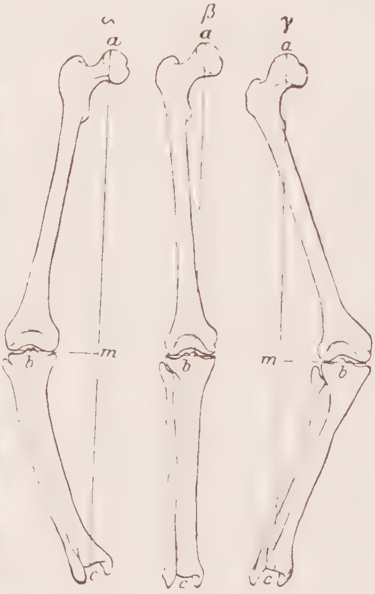


FIG. 662.

FIG. 658.—After v. Volkmann; reduced; A, footprint of normal foot; B, severe flat foot; C, unusually severe acquired flat foot.

FIGS. 659–661.—After v. Volkmann; I, paralytic pes equinus; II, paralytic pes calcaneus with hallux valgus; III, congenital pes calcaneo-valgus with very marked abduction kink, from a newborn child, due to intrauterine pressure. Position of foot during sleep.

FIG. 662.—After Mikulicz; right leg; a, genu varum; B, normal leg; Y, genu valgum; abc and amc, direction of gravity.

If these changes are present at birth, they can sometimes be blamed upon too little room in the uterus from too little amniotic fluid (Kustner believes this is true in but few cases; v. Volkmann). Julius Wolff contradicts absolutely the importance of oligohydramnia in the origin of typical congenital club foot. A mild degree of pes varus is physiological in the fetus. For the anatomy of the congenital club foot, see Pfrang. Pes varus and spina bifida occulta, consult under their respective headings.

Pes equinus, pes calcaneus and pes valgus are frequently the result of neurogenous paralyses, among which may be mentioned the spinal paralyses of childhood, and the rarer peripheral nerve diseases, which lead to so-called paralytic contractures. The paralytic pes equinus follows paralysis of all the muscles, as observed in a cadaver without rigor mortis. A paralytic pes calcaneus appears because the paralyzed muscles of the calf cannot hold the calcaneum in its proper position. Further deformities in structure are then brought about by the addition of the body weight. The deformity becomes permanent, not, as was formerly assumed, because of contracture of the antagonistic, non-paralyzed muscles (because it occurs when all the muscles are paralyzed), but from changes in the shape of the joint surfaces and the bones, and secondary nutritional shortening of the ligaments, muscles and tendons, (for example, the seemingly contracted Achilles tendon), (shown by v. Volkmann and Hueter).

Pes equinus may also be produced by an inflammation, for example, an abscess in the calf, inasmuch as the muscles are irritated into contractures; similarly a psoas abscess may lead to flexion of the hip joint (myopathic contracture).

The Chinese foot, according to H. Virchow, is an artificial pes equino-varo-calcaneus.

A pes planus acquisitus (acquired flat foot), is a flattening of the tissues of the foot from the pressure of the body weight. The tissues are held in tension partly by the muscles of the sole, partly by the posterior tibial muscle (which also lifts the internal edge of the foot-supination), which runs obliquely through the sole, and is wound around the talus (Henke). If this muscle is fatigued from long standing the weight of the body forces the foot in pronation and presses the arch inward; in fact, the arch may even become convex downward. The contour of the sole and the progressive flattening of the foot can be shown by imprints as demonstrated by v. Volkmann (fig. 658). The tarsal bones, in addition to being displaced, suffer changes in form and contour from these static circumstances (lit. v. Frisch). The rule is that muscles which no longer function undergo regressive fat changes; in flat foot these are the deep muscles of the sole (A. Hofmann).

Hallux valgus, adduction of the large toe, can usually be considered a static deformity in the sense of J. Wolff (Heubach), produced by the pressure of too pointed and too short shoes, in bare feet through active pressure of the foot against the floor. (v. Volkmann assumed erroneously that there was a primary deforming disease of the metatarso-phalangeal joint.) There also occurs a congenital hallux valgus; lit. by Zesas.

In **genu valgum,** knock knee, the thigh and the lower leg describe a blunt angle open externally; the knee joints tend to sink inward. In genu varum—sabre leg, bow-leg—the angle is open internally, the knee joints slide outward (fig. 662, a and y). The center of gravity in genu valgum is pushed so far externally, and in varum so far internally, that the supporting surfaces of the ends of the joints no longer touch. There is differentiated a genu valgum infantum and adolescentium, the first occurring in rachitic children when they first begin to walk. Genu valgum adolescentium is caused, according to Mikulicz, by late rickets (for rachitis tarda, see Looser and particularly Fromme, who emphasizes the importance of late rickets in various surgical diseases such as genu valgum and varum, coxa valga and vara, osteochondritis coxae, Schlatter's disease, pes planovalgus and kyphoscoliosis; see p. 1168). An important influence in the origin of the deformity is the weight of the body (long standing and improper posture); thus the combination of genu valgum, pes valgus (planus) is rather common. According to Mikulicz, the bowing occurs chiefly in the diaphyseal ends of the femur and the tibia; the joint is oblique because of irregular growth in the cartilage, and because of bowing of the obliquely developed diaphysis. Secondary causes are softness and uneven growth of the cartilage at the epiphyseal end, inasmuch as the cartilage in genu valgum, according to Wolff's theory (which, of course, is diametrically opposed to the Volkmann-Hueter pressure theory), becomes hypertrophic on the side (external) which is subjected to the stress, whereas, the non-used internal side, in which the normal growth-producing counter pressure—p. 1264—is lacking, becomes atrophic.

External and internal deformity of the elbow is called cubitus valgus and varus respectively. A mild degree of cubitus valgus is physiological (Mikulicz); in the woman it increases with puberty (Hubscher). Concerning humerus varus, see E. Bircher.

The normal shape and position of the neck of the femur and its head, depend upon the adjustment of various forces, chiefly the pressure of the weight of the body, the resistance of the bones, and the functional ability of the muscles. Deviations from the normal are:

(*a*) **Coxa vara** s. collum varum (E. Muller, Hofmeister and Kocher), a now frequently observed bending of the neck of the femur, consists of a diminution of the angle of the neck of the femur to the shaft (according to Lauenstein, it is normally 126° to 129°—see Harting), to a right or even an acute angle—Muller; the head is deeper. With kinking or bowing of the neck there is developed an abnormal situation of the leg in extension, adduction, and external rotation with shortening. Views differ concerning the causes of this bowing. The static factor is probably very important, particularly in coxa vara adolescentium (13th. to 18th. year), and probably occurs most frequently in hard working individuals who have grown very quickly (Sudeck). But whether or not long and severe strain alone is sufficient (according to Sprengel, Sudeck, Manz and others, it is not improbable), or if there must be added a particular elasticity of the bony tissue, must still be settled; possibly the latter is necessary (Hoessly). Views have been expressed concerning rickets, *i.e.*, late rickets—Hofmeister, Frosch, Fromme,—or "juvenile osteomalacia," as in a case of Kocher examined by Langhans. It is certain that in puerperal osteomalacia (Hofmeister), in senile osteoporosis, in ostitis fibrosa (Kuster), in osteomyelitis (Volkmann), in arthritis deformans, in traumata (Sudeck), a coxa vara may develop as well as in traumatic loosening of the epiphyses with improper healing (Sprengel). Coxa vara infantum which is much less common, and is noted during the first walking period (2 to 3 years), is believed by Hofmeister to be due to rickets. There also occurs a coxa vara congenita; the author, many years ago, described a severe case of this kind (figs. 12 and 14, angle below 90°, in his paper: Chondrodystrophia Hyperplastica, Z. B. 13, 1893). Later, Bosse described a coxa vara adnata chondrodystrophica more accurately. (For more details concerning coxa vara, see v. Frisch.) Kocher showed that the bowing is situated in a particular spot in the neighborhood of the epiphyseal lines; according to Sudeck, the youthful femur lacks a bony crust at this situation, which is later produced as a strengthening of the pull-bending system, and at which the intracapsular fractures of the neck occur in the femurs of old people. For the x-ray point of view, see Meyer.

(*b*) **Coxa valga** is the opposite of coxa vara; the angle of the neck of the femur is increased. This occurs: congenitally, after injuries, in congenital hip joint luxations, in rickets, osteomalacia, multiple exostoses, in genu valgum, in paralysis with pendulous legs, as well as in legs which cannot bear weight but are otherwise not paralyzed, after high amputations, etc., (Lauenstein, Tubby, Hofmeister, Th. Kolliker, Stieda, Kumaris, lit.).

Manus valga is a term used to describe a condition studied by Madelung, occurring in the hand, *i.e.*, the joints of the hand, consisting of "spontaneous luxation anteriorly," (Sauer, Putti, Siegrist, lit., P. Ewald, Melchior); according to Poncet and Leriche, it is merely a symptom caused by many processes such as rickets, ostitis, tuberculosis, which lead to bowing of the forearm, or to disease of the ligamentous apparatus of the joints of the hand.

Free Joint Bodies, Joint Mice.—These bodies have been mentioned a number of times in this chapter. As a resume, we may consider the various modes of origin of corpora libera articulorum:

Traumatic origin (push, fall), from normal cartilage or pieces of bone, the so-called cartilaginous and bony mice. They are particularly frequent in the knee and the elbow (Loison, Machol), joints in which periarticular bone formation frequently follows traumata. According to Barth, the bony part of the loose piece dies, while the cartilaginous part remains living, and has great growth ability (without perichondrium, there appears, not hyalin, but fibrous cartilage; Kappis, lit.). The surface from which it is broken off is covered by osteoid or more frequently by cartilaginous tissue, and then is covered by a connective tissue cloak.

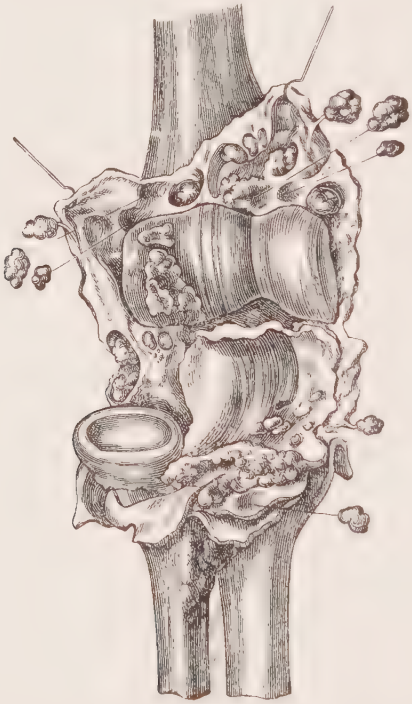


FIG. 663.—Numerous joint bodies in elbow joint (after Curveilhier); a rare case. These joint bodies occur more frequently in the knee (Billroth's Allg. Chir.).

The loosening of cartilaginous or bony edges or overgrown metaplastic cartilaginous or bony joint papillae in arthritis deformans (p. 1243). These joint bodies, often present in large number, reach the size of millet seeds to walnuts, and may show a mulberry-like surface. This type is also frequent in the knee and elbow joints (figs. 663 and 645).

According to Konig, free bodies may appear independent of trauma from a process designated by him "osteochondritis dissecans," characterized by the focal formation of granulation tissue, and consecutive cartilage and bone necrosis with subsequent loosening of shell-shaped bodies. Barth, on the other hand, believes these changes are purely traumatic, and are a gradual loosening of an incompletely fractured piece of a joint surface. Kappis also disagrees with the osteochondritis dissecans theory. Axhausen recognizes neither an independent osteochondritis dissecans nor a pure traumatic origin, but postulates a gradual loosening of a traumatic or otherwise injured joint focus; he therefore takes a middle position. Buchner and Rieger believe it is physically impossible for a joint mouse to originate from the action of external force on a sound joint, but do think that obstruction to vessels from fat embolism with secondary dissection of the damaged area, is a quite probable cause (Axhausen). The origin of joint mice is therefore a question still obscure.

Loose intraarticular exostoses.

The free bodies mentioned above are the joint mice of the surgeon.

Parts of capsule tumors in chondromatosis of the joint.

The loosening of fibrous or lipomatous joint papillae (p. 1243). Rice bodies (corpora oryzoidea), have been discussed under joint tuberculosis (p. 1257). Fibrin coming from hemorrhages or inflammations. Even foreign bodies from external sources may become corpora libera.

If the free bodies are fairly dense, they have a tendency to become smoothed off; when they are soft they become flat. Occasionally they undergo petrifaction.

(For experimental data, see, among others, Rimann.) Lit. concerning joint mice by Martens, Kirschner, Brehm, Neumann and Suter, Troell, Axhausen, Barth, Kappis.

CHAPTER VII

THE ADRENAL GLANDS

Anatomy.—Each adrenal gland is enclosed in a capsule from which septa with numerous blood vessels pass into its interior. The blood supply comes from three sources, the superior adrenal artery which springs from the inferior diaphragmatic, the middle suprarenal artery coming from the aorta, and the inconstant inferior suprarenal artery which arises either from the renal artery or one of its branches, from the kidney itself, from the spermatic artery or from the aorta. (Beitzke.) The veins, especially rich in smooth muscle fibres (Maresch), unite in the medulla to form the principal vein, the suprarenal. The cortex, easily differentiated from the medulla, consists of epithelial cell-groups between which are abundant thin-walled blood capillaries. There are three rather poorly differentiated zones, the outer, zona glomerulosa, contains round or oblong masses of epithelial cells, and represents the cortical germ layer which atrophies in old age, (Landau); the middle zone, zona fasciculata, consisting of vertical anastomosing pillars resembling columns of liver cells is composed of polygonal epithelium with transparent cell substance in which are frequently found fat droplets of which about 60% are doubly refractive lipoid granules; (cholesterin ester; for more exact data see Biedl, Landau, lit.). After extraction by alcohol, ether, etc., the cells appear highly vacuolated. Between the pillars are connective tissue septa. This is the broadest zone and from the tenth year onward is normally of yellowish color. The inner, or reticular zone is composed of various sized cell groups anastomosing with each other. The cells are polyhedral in form, with more or less rounded corners and are not very transparent; with age they become increasingly granular, diffusely yellow or pigmented brownish yellow to dark brown, (pigment zone), and rich in lecithin and fat. The pigment is classed with the lipofuscins or catabolism pigments (see Tuczek). This zone forms a dark colored band which is set off in sharp contrast from the light gray gelatinous translucent medulla. In the *medulla* are round or oval strands of transparent cells in a net-like arrangement; their nuclei are vesicular, their shape polyhedral, cylindrical or branching, and although they have no nerve prolongations, they belong to the "chromaffin" (Koch), or "chromophil" (Stilling), system since they are stained yellow-brown by solutions of chromic acid salts.[1] These cells furthermore contain sharply circumscribed granules, easily soluble in water or alcohol, and on these seem to depend the specific reactions such as the chrome brown, iron green, the Colin's reaction, (intensive green coloration under the influence of iron oxide salts), and the oxidase reaction (see p. 196; see lit. by Poll); ("secretion granules in the medullary cells," see Scheel).

Chromaffin cells are also found in the ganglia and larger nerves of the sympathetic, and in the paraganglia,—globular structures distinct from the sympathetic ganglia consisting of a ganglion-like body composed of chromaffin tissue. Kohn (lit.) numbers in the chromaffin system the medullary substance of the adrenals, the paired carotid glands, (see p. 330), the coccygeal gland, which is a few millimeters long and lies in contact with the terminal end of the median sacral artery at the last caudal vertebra, as well as the organs of Zuckerkandl often found along the large abdominal arteries. Chromaffin cells are also found in the epididymis and in the paroophoron. The expression "chromaffin-system" is often heard. Adrenalin, (see below), is the specific product of the chromaffin cells.

Numerous capillaries and venous plexuses are located within the medulla. The large venous trunks lie in the center of the adrenal, while a meshwork of lymph vessels is found in the capsule and in the septa as well as surrounding the central veins. Nerves which penetrate the capsule are very numerous, and consist of non-medullated fibres, mostly from the celiac plexus. They form a meshwork in the reticular zone and particularly in the medulla, in which they are extremely numerous surrounding each single cell. In the medulla are also groups of melanotic pigmented ganglion cells arising, according to Wiesel, as in the chromaffin system, *i.e.*, primarily from "sympathetic formative cells,"—sympathogonias (Poll),—which are small and dark, but do not yet contain chromaffin.

In size and color the adrenal glands vary markedly. In the young the cortex is brownish gray but it becomes more and more yellow through fat absorption. In advanced age, the total size decreases and the fat is limited to a few foci. The average weight of both adrenals of adults is 11.6 g. for males, 10.6 g. for females. In the negro the adrenals are said to be exceptionally large and rich in pigment, and this has led to the supposition of a relation of this organ to dermal pigmentation, but according to Tuczek, these statements are erroneous; "the cortical pigment has really no relation to skin pigment which belongs to the melanin bodies."

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[1] Place fresh pieces for 24 hrs. in 3.5% potassium bichromate solution or into a mixture of 90 parts of this with 10 parts of a 40% formalin solution, the usual commercial kind (Kohn).

(Tuczek.) Nevertheless the adrenals may exert some sort of regulatory influence on the pigment metabolism of the skin. (Meirowsky.)

Their position corresponds to the lower half of the eleventh and the upper half of the twelfth thoracic vertebrae, and they lie medially against the upper poles of the kidneys. .

Development of the Adrenals.- This was long a disputed point, (see lit.), until Wiesel formulated the teaching which is now steadily gaining acceptance that the adrenals are built up from two completely different anlage or tissue systems. The cortex develops from coelomic epithelium, *i.e.*, from the mesoderm, while the medullary substance is formed from the ganglionic germ layer of the sympathetic, *i.e.*, ectoderm. Neuro-ectodermal formative cells of the sympathetic wander into the inner layers of the epithelial substance, and transform themselves mostly into the later chromaffin medullary cells, but a small number develop into ganglion cells.

The secretory products of this organ, according to some, are carried away by the lymphatics; according to Gottschau, they are given in granular form into the venous blood. At any rate it is not conducted through efferent ducts, and therefore the term internal secretion is used. The cellular activity of the adrenals has a specific influence on the sympathetic nervous system, and there is elaborated synthetically a substance essential for its normal nutrition and the maintainance of normal tonus. It follows that suprarenal activity exerts an influence upon the heart, and is of great importance in the maintainance of tonicity of vessel musculature and sustained tonic innervation of all vegetative organs depending on the sympathetics. On the other hand, it is assumed that the cortex, the function of which is practically unknown, detoxifies, probably by its lipoids, not only metabolic products such as result from muscular action, but also bacterial toxins and simple poisons such as metals (lit. by Neusser, more complete by Biedl). In this way, the adrenals influence the organism as a whole, and are necessary to life. Adrenalin, produced by the adrenals, and continuously carried into the blood stream is a product of the chromaffin cells of the medulla. It serves to regulate vascular tonus, and increases arterial pressure by increase of peripheral resistance consequent on contraction of the lumen of arterioles; those of the kidneys are exceptionally sensitive. It causes contraction of the smooth muscle fibers of the uterus, but inhibits intestinal tonus. Its influence on sugar metabolism is shown by the glycosuria following its intravenous injection, probably from mobilization of the carbohydrates of the liver. It is thought possible that Claude Bernard's diabetic puncture also influences the adrenals; (experimental injury caused to arterial walls by adrenalin, on p. 138).

A number of chemical color reactions with adrenalin, have been discovered and methods for its quantitative determination in tissues and fluids (blood, etc.) have been worked out, also a biological test (Meltzer-Ehrmann), whereby the smallest amounts of adrenalin are detected by mydriasis, (pupillary enlargement), in the enucleated eye of the frog. Schmorl-Ingier, Elliot, Lucksch and others have reported the adrenalin content of the adrenals in health (approximately 8 mg., Lucksch), and in disease. The greatest reduction, even total absence, was found in Addison's disease, and in burns these conditions are approximated, according to Lucksch. On the other hand, increase was found in nephritis, at times in cases of sudden death, and in healthy suicides. With a high adrenalin content, a correspondingly high lipoid content may occur as found in circulatory disturbances such as contracted kidneys, heart failure, etc. This parallelism is further accentuated by the finding in infections, (see Lucksch), of a reduction of both adrenalin and lipoid. (Landau-McNee.)

Relations to Other Organs.—The relations of the adrenals to other endocrine glands are complex; thus Falta, Eppinger and Rudinger find inhibiting factors between the adrenals and the pancreas; and between the adrenals and the thyroid there are said to be mutual stimulatory relations. (Details and lit. by Poll-Beitzke-Ehrmann and by Biedl.) Hyperplasia of the adrenal cortex in acromegaly is considered a consequence of the hyperactivity of the eosinophile cells in the hypophysis cerebri, and the decrease or hypoplasia of these same cells is, conversely, considered the cause of atrophy of the adrenal cortex. (Kraus.) There is at times a correlation between changes in the adrenals and the reproductive glands; thus Marchand found in a case of pseudohermaphroditism externa femina with rudimentary development of the ovaries, a marked hyperplasia of the adrenals, and an accessory adrenal, (size of a testicle), in the broad ligament; (for newer literature see under pseudohermaphroditism). See Mathias, p. 1291, in reference to heterologous sex characters developed by those with hypernephromas. For alterations of the adrenals, broadening of the cortex after castration, see Schenk, Kolmer, Kolde, lit. According to Leupold, (lit.), after experimental extirpation of the adrenals, severe injury to the testicular reproductive cells takes place, while the cells of Sertoli and Leydig apparently are not affected; according to Novak, (lit.), sexual development is retarded in animals without adrenals. Aschoff, Stoerk, Wiesel, Kolde lit. etc., report medullary hyperplasia in pregnancy, but these findings are not constant. On the other hand, an enlargement of the cortex is recognized in pregnancy, depending especially on increase of fat in the fascicular zone, and on true hyperplasia of the zona glomerulosa. (H. Sternberg—lit.)

Different degrees of **hypoplasia** of the adrenals, especially of their cortex, up to uni- or bilateral absence are mostly found in combination with malformations of the brain such as hemi-anencephly, hydranencephaly and syncephaly. (Lit. by Miloslavich, more details regarding the adrenals in anencephales by Kern, Veit, Hirschfeld, Nussbaum, R. Meyer, Landau.) The question arises: is the adrenal hypoplasia dependant on the malformation of the brain or do both represent coordinated developmental disturbances? According to Zander, hypoplastic adrenals occur only with defects of the frontal brain; malformations of the genito-urinary system often coexist.

Unilateral Aplasia.—Absence of an adrenal gland in an otherwise well formed body is rare. (Miloslavich.) **Total absence** of both adrenals is very rare. (Miloslavich, lit., Strauss.) According to Wiesel, hypoplasia of the chromaffin system makes the organism less resistant, and sudden deaths may follow relatively slight injury. (See also p. 500 hypoplasia of the chromaffin system and status lymphaticus; also lit. by Strauss.)

In animals which were partially nephrectomized, Schur and Wiesel saw hyperplasia of the adrenals and increase of adrenalin in the blood. Under "contracted kidney" are reports of supposed cortical hypertrophy of the adrenals. The adrenals and rachitis and osteomalacia are discussed on p. 1160. (Schur and Wiesel, Hornowski.) The claim that chloroform and ether narcosis prove injurious and after a time deplete the chromaffin cells as shown anatomically by the poor chromaffin color reaction of the adrenal medulla, could not be verified by others (Schwartzwald), but it has been quantitatively demonstrated in case of death occurring within twenty-four hours after narcosis that a slight decrease of adrenalin content is present. (Schmorl-Ingier.)

Compensatory hypertrophy of one adrenal occurs after experimental extirpation, (Stilling, see Simmonds), or pathological destruction of the other (Hanau, Simmonds; in tuberculosis the author saw one 19 gm. in weight). In older rabbits the power of regeneration is lost or is only very slight. (Carraro and Kuznitzky.) If the adrenals are destroyed, *e.g.*, by tuberculous caseation, it is possible that accessory genital adrenals may enlarge compensatorily. (Roth, Pilliet.) Similar results have been found experimentally after removal of both adrenals. (Stilling, Hanau, Wiesel.) In reference to acquired hypertrophy, see Roessle.

Displacements (dystopias) of adrenals may be congenital, (*a*) total subcapsular, (*b*) partial subcapsular position in the kidney; or acquired, with extracapsular, position, adhesion of capsule to the kidney or liver. (Miloslavich, lit.) See Lucksch in reference to the fusion of both adrenals into a butterfly-like structure, analogous to the horseshoe kidney.

Accessory cortical nodules occur frequently in the fetus and the newborn, either in the capsule or arising pedunculated from the cortex. Landau considers them an expression of intensive surface growth, and saw them more frequently during the first year of life, while from the second to the tenth year they are rare, probably because they become incorporated into the growing organ. In the adult, they again bud forth more frequently or become snared off by inflammatory processes.

Accessory adrenals are composed mostly of cortical substance, and vary in size from a hemp seed to a cherry. They occur (1) as real fragments of the main gland in its immediate vicinity, in the suprarenal and renal region, in the connective tissue, in the solar plexus, or in or beneath the renal capsule, as well as in the kidney substance. (Grawitz.) They may be flattened out on the renal surface, and those located in the renal parenchyma probably correspond in their locality to the furrows of former renculi. To this class also belong accessory adrenals underneath the capsule of the posterior surface of the right lobe of the liver (Schmorl), in the hepato-duodenal ligament (Eggeling), and also perhaps in the pancreas (Ribbert). (2) Accessory suprarenal glands occur distal to the lower renal pole, even at a considerable distance, quite frequently in the vicinity of the sexual glands (genital sphere). Aichel calls this second group "Marchand's adrenals," and considers them independent organs. They are found within the broad ligament, (Marchand), on the spermatic vessels, in the inguinal canal, on the spermatic cord between testicle and epididymis (Dagonet, Chiari), in the corpora Highmori of the testis (Roth), on the epididymis, (Wiesel), in retroperitoneal connective tissue, on the internal spermatic vein in males (Michael), (lit. by Aichel and lit. p. 1278). (For the pathological significance of Marchand's adrenals see Pick, and also Biedl, lit.)

After **transplantation,** the cortical substance may survive permanently (Stilling). Schmieden and v. Haberer and Stoerk successfully transplanted the suprarenal gland with a pedicle into the kidney. The **extirpation** of too large an amount of adrenal tissue, causes the death of the animal with a typical symptom complex. According to Moussu and Le Play's experiments, in dogs and sheep, a small portion of cortex and medulla is sufficient to preserve life (see lit. by Biedl).

Softening.—The yellow cortical layer in the pigment zone frequently separates into layers and forms a brown coated flattened cavity not to be mistaken for a cyst. This is seen particularly in senile atrophic adrenals and is usually regarded as post-mortem softening, but recently this explanation has been disputed. Thus, according to Materna (lit.), these processes are not post-mortem autolysis, but intravital softening and splitting in the zona reticularis, the result of acute infections as well as tuberculosis. This question needs further investigation.

Ingier-schmorl spoke of cavity formation in the medullary substance and between that and cortex, which might be favored by the squeezing and pressure of removal at autopsy.

Hemorrhages occur in the hemorrhagic diatheses, in leukemia, in infectious diseases, for instance, diphtheria by infective emboli (Simmonds), in death by asphyxia, during birth, (Doerner, B. Schultze), in marasmic thrombosis of the veins especially in children, but also in adults (see Lissauer), and subsequent to trauma including birth trauma. Small hemorrhages may be confined to the inner part of the cortex. Larger hemorrhages sometimes lead to immense tumor-like hematomas; these are more frequent in the right adrenal. They may produce death not only through rupture, but sudden death with symptoms of poisoning, and marked lowering of blood pressure is not unusual. Kolisko, finding them in burns and scalds, believes they lend support to the intoxication theory in death from burns. (See also Kucharski, and lit. in appendix.) Only rarely does organization and encapsulation, calcification or ossification, or cystic transformation occur.

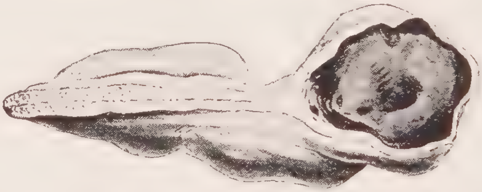

FIG. 664.—Cyst in adrenal gland due to hemorrhage; nat. size.

Inflammation.—Behavior during **infections:** Simple inflammations are rare. In infections, perivascular and interstitial increase of lymphocytic infiltration is observed. (Lit. by Goldschmidt.) Scheel described an interstitial edema with degeneration of the cortical cells in febrile diseases. Swelling of the cortex may occur in addition. Diedrich (lit.) always found changes, chiefly cortical, in fatal wound infections, especially in severe toxemias such as in gas edema and peritonitis. There were loss of lipoids or extensive cell injuries such as vacuolation, honey-combed swelling, disintegration, acinus-like lumena, etc.; vascular disturbances, such as hyperemia, hemorrhages, collections of leucocytes and migrations, up to focal infiltrations, autolytic phenomena, even thrombus formation, have also been found. Dietrich believes this shows that the cortex binds certain toxic substances which flow through the body. (Chvostek.) There is sometimes abscess formation with total destruction of the gland, sometimes also cicatricial atrophy, the latter chiefly in tuberculosis. Of specific inflammations luetic conditions are rare, but tuberculosis is of great importance. (See Thomas as to changes in the adrenals in children in infections.)

Tuberculosis of the adrenals takes the form of miliary nodules in general miliary tuberculosis, or the form of a chronic caseous fibrous inflammation. In the latter condition the adrenals enlarge, sometimes to the size of a plum or a small hen's egg (Virchow); they are firm, often actually hard, and irregularly nodular. On section, the capsule is thickened and adherent to neighboring tissues; the parenchyma is partly or completely replaced by cheesy, yellow, firm, nodular foci or by puriform, sometimes cavernous soft masses surrounded by cicatricial connective tissue. The caseous areas may calcify. One or both glands may be involved. The tuberculosis is usually secondary, and according to Tendeloo probably is of lymphogenous origin from pulmonary or intestinal sources, etc. It is rarely primary, but may be the only tuberculous infection of the body. It even occurs congenitally.

It is frequently the starting point of tuberculous peritonitis, or more rarely, of general miliary tuberculosis, the infective material being distributed through tubercles of the veins, or by caseous ulceration into the adrenal vein. (Hanau.) But it may remain localized, and even heal completely. (Simmonds.) De Vecci produced tuberculosis of the adrenals experimentally.

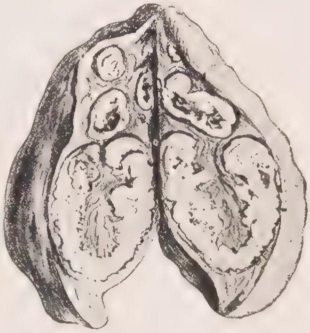

FIG. 665.—Tuberculosis of adrenal (the other was quite similar) of man 50 years old. Marked pigmentation of skin, caseous mesenteric lymph nodes, cavernous tuberculosis of kidney; 5/6 nat. size.

A frequent, but by no means constant finding in **Addison's disease** is tuberculosis of the adrenals. The process generally begins in the medulla which is replaced in toto by caseous masses; occasionally, even large parts of the cortex escape (Tendeloo, Loeffler). The disease is fatal, usually chronic, rarely acute; it favors males; in typical cases there is bronzing of the skin and those mucous membranes which are exposed to light. Increasing anemia, general asthenia, and a remarkable weakness of heart action soon occur. Disturbances of the alimentary tract and of the cerebral nervous system are added and the picture often suggests severe poisoning. But the adrenal insufficiency may cause sudden death from lowering of blood pressure—so-called minute-heart death. (See, among others, Steiger.) The discoloration of the skin which is diffuse or in spots, usually begins in the areas exposed to light while the soles of the feet, nail-beds and palms of the hands as well as the sclera are unaffected. It shades from yellow and light brown to a dark greenish-brown, smoke-gray, or blackish-brown. The regions which are normally pigmented and those upon which the pressure of clothing is especially marked, for instance, below the garters, are often remarkably dark. The skin of the lips and the mucosa of the cheeks are often blotched with dark pigmentation, brown, spotted, striped, pointed, and irregularly demarcated. (Melanoplakia.) Similarly the conjunctiva, the preputial mucosa and the vaginal introitus show brown discoloration. The pigment is most thickly deposited in the deepest layers of the rété Malpighii, but is also found in the upper layers of the corium; nucleated pigmented connective tissue cells may push prolongations between the epithelium. This may be only an increase in the mother substances of normal skin pigment, which becomes oxidized by a pigment-forming ferment of the skin oxydase, (Bloch and Loeffler; see also Bittorf who accepts the theory of an increase of the oxydase). Heudorfer, who does not share Bloch's conception of pigment formation, explains the

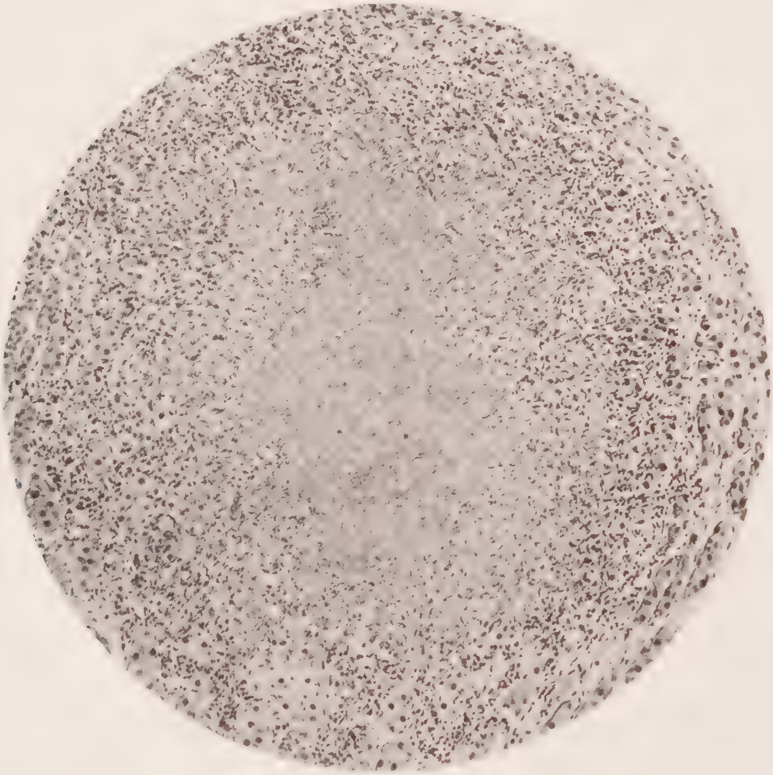

Fig. 666.—Miliary tuberculosis of the adrenal in a patient 24 years old. This was merely part of a general miliary tuberculosis from which the patient succumbed. The source was probably in the lungs. This type of tuberculosis of the adrenal is distinguished sharply from the tuberculosis which produces Addison's disease. The latter, as a rule, shows tuberculosis in other organs but is distinguished by being exceptionally severe and standing out as a distinct entity and not merely as part of a generalized tuberculosis. × 120. L. H. #147.

pigmentation on the grounds of increased skin activity representing an attempt to compensate for the elimination of the adrenals. Cases of adrenal cachexia without bronzing of the skin are termed atypical. The diagnosis of Addison's disease is thus not made. The author saw two such cases which were very severe and rapid in their course giving the appearance of a poisoning or toxemia; there was caseation of the entire adrenals. According to Leichtenstern bronzing of the skin is but a minor symptom of Addison's disease and is to be regarded only as a secondary consideration; according to Leube, it is the only objective symptom, and according to Lewin, it is the most important one. Many speak of a melasma suprarenale, (see Pospelow), and this all shows how opinionated is the clinical aspect of the disease. Finally, the deepest sort of bronzing and pigmentation of the skin and mucous membranes occurs in other diseases and melanoplakia likewise, without disease of the adrenals. Liver diseases, carcinoma, especially of the stomach, might be mentioned. None of the other symptoms of Addison's disease appears. Other lesions of the adrenals, usually, but not always, bilateral have occasionally resulted in Addison's disease. These are: marked simple atrophy seen by the author in a case of Addison's disease with bronzing of the skin in a 24 year old girl, in whom in consequence of cortical atrophy the adrenals were reduced to two flat, almost translucent, tags with a maximum thickness of 2 mm.; chronic interstitial inflammation leading to atrophy in which lues is perhaps a factor (lit. by Simmonds, Lucksch); chronic hemorrhagic inflammation of the adrenal cortex with intact medulla, and leading to gradual atrophy (Fahr and Reiche, lit.); tumors, usually malignant, either primary or secondary (see Bittorf, denied by Oehlecker); finally hemorrhages, thrombosis of the adrenal veins (Straub, Bittorf), cysts and amyloid infiltration (very rare, see Bittorf). Many attach the greatest importance to cortical atrophy. (Lucksch, Roessle, compare, on the other hand, Bannwart.) Rare cases of total suprarenal aplasia in adults with late developing Addison's disease are explained by assuming that accessory adrenals functioned vicariously for a time. (Strauss.) On the other hand, these same processes sometimes are not accompanied by Addison's disease, and cases are seen in which both adrenals are completely invaded by large metastatic sarcomatous nodules such as one seen by the author in a case of melanotic skin sarcoma, and one by Maclachlan, in which Addison's disease had not developed. It is necessary to think of vicarious activity of accessory adrenals, (Pilliet), or of other parts of the chromaffin system. Lewin's statistics comprising 684 cases to the year 1892, show that the adrenals remained unchanged in typical Addison's disease with bronzing of skin in 12%. But it was not satisfactorily proved that the more minute microscopic changes in the chromaffin cells had been sufficiently studied.

In addition to caseation of the adrenals, changes in the nervous system of the region are sometimes observed in Addison's disease, especially lesions in the abdominal sympathetic and its large ganglia, principally the solar plexus; usually however changes in this system are absent. Many authors attach great importance to these changes, when found, consisting of fatty degeneration, thickening of vessels, inflammatory foci, hemorrhages, etc., but according to Kahlden, this view has not been substantiated. Indeed everything points to a dysfunction of the adrenals themselves with the underlying anatomical change the caseation as the cause of Addison's disease, but at present it is impossible to state whether cortex or medulla, or both are responsible. (Lit. by Bittorf, & Neusser a. Wiesel Bannwart. other lit. in appendix.)

In the newborn, **syphilis** of the adrenals may appear as a diffuse interstitial inflammation with induration, and rarely as gummas. Both are observed in acquired syphilis.

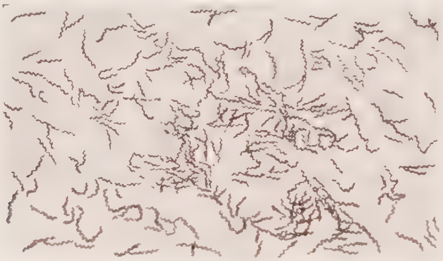

FIG. 667.—Large numbers of spirochetae pallida in adrenals in congenital syphilis (Levaditi silver stain); oil immersion 1/12.

Simmonds described diffuse interstitial inflammation ending in atrophy, and emphasizes in a second communication that the usual form is a perihypernephritis extending from the capsule to the cortex or vice versa.

In congenital lues, it is often quite easy to demonstrate enormous numbers of spirochetae pallida in the adrenals, even when the organ shows little or no ordinary histological changes.

Amyloid degeneration is frequent in general amyloidosis. The organ becomes thicker, harder, glassy and pale gray in color. The amyloid is deposited in the walls of the blood vessels and in the connective tissue; the parts swell, and pressure produces atrophy of the cell columns of the parenchyma. The cortex, especially its inner half is most affected; the medulla is rarely invaded and then only in the walls of single vessels (Scheel, lit.). According to Peters, the amyloid is deposited around as well as between the capillaries and the parenchymatous cells, causing atrophy of the latter by pressure or insufficient nutrition. Peters often found epi- and peri-cellular amyloid deposits predominating over the interstitial pericapillary infiltration.

Tumors and Parasites

Primary tumors are at times bilateral. There are two main groups: (I) tumors of the cortex; (II) tumors of the medulla. In the first group are differentiated diffuse hyperplasias (rare), and nodular hyperplasias, the latter were called by Virchow: strumae suprarenales; by others, adenomas; by Birch-Hirschfeld, hypernephromas. These nodules are fairly well differentiated from the displaced adjacent parenchyma, and are of the color of the cortex, *i.e.*, sulphur yellow, lemon yellow, green, and from hemorrhage spotted red, brownish-red or brownish. They may grow to the size of a cherry and more, and consist, microscopically, of adrenal tissue usually of cortical architecture, often with marked fat infiltration, *i.e.*, with doubly refracting substances and there is often glycogen within the cells. Typical cortical hypernephromas or adenomas are very frequent, often differentiated from the surrounding tissue by the amount of their lipoid content. They are often considered "hamartomas," tumor-like malformations (see v. Gierke), but their increasing frequency with advancing age makes this improbable. The typical medullary hypernephromas situated within the medulla may have their origin in those misplaced cortical rests which are so frequently found in the medulla. The adenomas in their progressive development imitate the cellular arrangement of the cortex (demonstration of adrenalin in hypernephroma p. 1279, see among others, Orth).

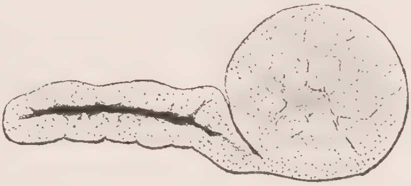

FIG. 668.—Nodular hyperplasia, so-called struma, hypernephroma of adrenal; nat. size.

Tumors of the adrenal medulla are of special interest. They have their analogy in other tumors of the sympathetic nerves, (see details under nerves), and of the paraganglia (p. 1277). Marchand first showed that such tumors in rare cases may spring from the sympathetic portion of the adrenals. Three groups may be differentiated: (1) neuroblastomas, (2) ganglioneuromas, (3) paragangliomas. The relationship of these variously named tumors is established by the fact that the embryonic sympathetic cell, the cell from which the sympathetic system is built up, (sympathogonia), may differentiate in two directions: (*a*) into **parasympathetic, chromaffin cells** which normally are the chromaffin auxiliary structures of the sympathetic—the paraganglia, and (*b*) the **sympathoblast cells,** nerve cells which normally become sympathetic ganglia. Alezais and Peron designate tumors of the type of the paraganglia and sympathetic ganglia, *i.e.*, completed tissue, as paragangliomas and ganglioneuromas respectively, and such tumors which correspond to an earlier stage, *i.e.*, to less differentiated cells, they call parasympathomas and sympathoblastomas respectively.

Neuroblastomas (sympathoblastomas; sympathogonioma; according to Pick, ganglioma embryonale sympatheticum, or sympathoma embryonale), correspond to the undeveloped sympathetic cells, (prestage, formative cells (Wiesel) of the sympathetics). They consist of round cells poor in protoplasm with a finely reticulated ground substance. Herxheimer (lit.) could follow the differentiation to the formation of neurofibrils. These tumors appear congenitally, or at least only in children, (exception: case of Barnewitz), and are exceedingly malignant, (exception: case of Marchand). They infiltrate, metastasize to liver, lymph nodes, cranium, etc. (see also Kohler). But Pick points out that multiple primary tumors may develop simultaneously in the adrenal, liver, and elsewhere, a fact of importance in diagnosing metastases.

Those tumors which have been described as gliomas of the adrenal, (Kuster, Lapointe and Lecene), belong, as first emphasized by Wiesel, to the neuroblastomas, (see also Wright, lit.), and notwithstanding the arguments of Schilder, (case of "malignant glioma" of the right border fibre of the sympathetic), this conception is shared by most workers. (See Pick, lit. Herxheimer, Barnewitz, lit.)

The two following forms usually composed of fully differentiated tissue, spring from the sympathogonias, the common cell beginnings.

1. **Ganglionneuromas** (see fig. under nerves). According to Landau, it is necessary to differentiate between those with low-grade tissue differentiation, of malignant character, and selecting the young, and the slow-growing, benign type with fully ripened cells which make up by far the greater number. These latter consist of mature sympathetic cells, *i.e.*, ganglion cells, which may also be polynuclear and degenerated and with non-medullated and medullated nerve fibres with Schwann's sheaths. With increasing differentiation of the tumor tissue, which, generally speaking, increases with the age of the individuals affected, their malignancy decreases. (Landau.) Females are more prone to these tumors than males. Youth is favored, but no age is spared. Their size varies from that of a plum to the size of a fist or even a man's head. Sometimes they are accidental post-mortem findings. (See also Bruckanow, Fabris, Oberndorfer, Hook, lit., Geller, Wassmund, lit., Jaffe, Berner.)

2. **Paragangliomas** are chromaffin tumors consisting of fully mature chromaffin cells. They are rare. These also have fewer differentiating prestages. Those fully matured, in similarity to the ganglioneuromas, are benign, and consist of chromaffin polyhedric cells containing some glycogen but no lipoids, and are alveolar in arrangement. The paragangliomas may also be cystic, and are then spoken of as **chromaffin medullary cystic strumas** of the adrenals. (Suzuki, Neusser-Wiesel. Hedinger, Wegelin, Herde, Thomas, lit.)

The term paraganglioma is also used in connection with the carotid gland, coccygeal gland, and the organ of Zuckerkandl, because these glands have the same origin as the adrenals. (See above.) The tumors of these organs also contain chromaffin cells although much less in number than those of the adrenals, and show alveolar structure. The author and Ruppanner for this reason named them alveolar tumors. (See page 330.)

Cyst formation takes place in consequence of breaking down of tumor tissue, or from a hemorrhage after which the so-called blood cysts may attain considerable size. (Fig. 664; lit. by Gjorgjewitsch.) Lymph cysts, in part lymphangiectasias (Oberndorfer, de Vecchi, lit. Nowicky), in part cystic lymphangiomas (Sick lit.; Preusse), are very rare. Hemangiomas also are rare (s. Volkmuth); Lucksch, (lit.) mentions an hemangio-endothelioma.

Lipomas have been seen in isolated cases. (Bruchanow, Marchetti.)

Sarcomas.—There are melanotic and pigmentless spindle-cell sarcomas, angiosarcomas, myxosarcomas, and at times hemorrhagic sarcomas, as also lymphosarcomas which are rare. Viewed superficially, neuroblastomas (sympathogoniomas) may be mistaken for round cell sarcomas, and pure neurocytomas (see under nerves) may be mistaken for spindle cell sarcomas. They may occur congenitally and in early youth; they have occasionally been bilateral. (de Ruyder.) Descriptions of bilateral melanotic sarcomas, melanomas, and melanotic adenomas have also appeared, (Davidson, Goldzieher, J. Schmitt, Lucksch, Molnar, Maclachlan). Ribbert thinks that in Davison's and Schmitt's cases of bilateral melanotic sarcoma, they were dealing with metastases from skin tumors. Many tumors described as sarcomas probably belong to the class of **malignant hypernephromas.**

Transitions have been observed from nodular hyperplasias to malignant cellular tumors, some with alveolar architecture, some of polymorphocellular sarcoma character but none with actual epithelial character. Benecke speaks of adenosarcoma, while Marchand calls them simply malignant tumor. Lasagna designated them as atypical adrenal tumors at an earlier date, and Beitzke and Ciaccio called them carcinomas. Roccavilla speaks of a sarcomatoid malignant adenoepithelioma, while

Ciaccio emphasizes the special importance of siderophile cells and oxyphile substance (see page 1276) in the diagnosis of epithelial adrenal tumors. According to Birch-Hirschfeld the tumors should be called **malignant hypernephromas** on account of their histological structure, which is neither identical with sarcoma nor carcinoma, but shows many similarities to adrenal tissue. He gave this tumor its name, "hypernephroma." (Grundriss. der allg. path. 1892.) This expression is convenient even if it does not follow the general rule of naming a tumor from its tissue character and not from the organ in which it arises. (See also Orth.) Histologically their appearance varies. Differentiation must be made between a typical and an atypical form, just as in malignant chorioepithelioma. In its typical form, there is great similarity to adrenal structure, because of the arrangement of the cells into columns, slender pillars, strands and clumps within a framework of capillaries. A yellow or whitish-yellow color is imparted by the massing of fat granules or of doubly refracting lipoids and of glycogen. After extraction of these substances in histological preparations, a honey-combed transparent appearance is imparted to the cell protoplasm. Its malignancy is shown by invasion into veins and the production of metastases. In the atypical form the structure is much more irregular. The cells are larger, polymorphous and poorly outlined; the structure is in parts alveolar as in carcinomas; elsewhere there are polymorphous cells and among them enormous giant cells, up to 150 microns, with giant nuclei. The author described such a case which led to an exceptional metastasis to the uterus. Alveolar arrangement is entirely absent. The picture suggests sarcoma especially that of the metastases and recurrences, a finding which likewise occurs in the renal atypical malignant hypernephromas (see Loening, and then compare Neuhauser); but again in the same tumor there are areas which are identical with typical hypernephromas, suggesting adrenal structure, and which also contain single and doubly refracting fats and glycogen. Gland-like, spaces are also seen within (Asanazy, lit.), a statement which, however has been denied; (Zehbe, see also Prym who speaks of pseudo-gland spaces). These tumors grow to considerable size, and may be increased by hemorrhages. They are very malignant, rupture relatively frequently and early into the veins and quickly form metastases. Between the typical and atypical hypernephromas just as in the corresponding renal tumors, there are often no sharp demarcations as pointed out by Sabolotnow; and typical ones may become malignant (see above lit. by Orthmann).

The metastases may at times completely dominate the picture, since invasion of the veins occurs early, (comp. Oehlecker, lit.; compare the similar behavior of renal hypernephromas).

Misplaced adrenal rests may also participate in tumor formation. (Beneke.)

If accessory adrenals change into tumors (see p. 1281), they are spoken of as heterotopic hypernephromas, and differentiated histologically into typical and atypical. If such a tumor develops in the genitalia, it is difficult to accept its origin from the kidney, where Stoerk believes all heterotopic hypernephromas begin. In such a case Adrian saw numerous punctate pigment spots in the skin as occurs only in adrenal tumors.

Interesting problems are presented by certain occasional relations of the adrenal neoplasms, especially hypernephromas, to the genitals. Although they do not occur with greater frequency in women, (see also Oehlecker), in this sex they lead more frequently to abnormalities of sex function, (see Glynn, lit.), especially before the menopause. There occur a weakening of certain feminine characteristics and a development of masculinity. In some cases in the male, there have been sexual precocity (lit. Biedl, Boehm), and rarely a change of sex characteristics or femininization. (Comp. Glynn and Hewetson, Mathias.) It was pointed out on page 1279 that there is an occasional coincidence of pseudo-hermaphroditism with adrenal cortex hyperplasia.

Secondary Tumors.—Sarcomas and carcinomas are not rare, carried in by lymphatics or blood vessels. In a seventy-one year old woman who died three years after amputation of the breast for carcinoma, the author saw in the center of a sulphur yellow adrenal adenoma the size of a mandarin, a grayish-red metastatic carcinoma nodule the size of a cherry, softened and hemorrhagic in the center. Of **parasites,** the rare echinococcus hydatid invasion may be mentioned.

CHAPTER VIII

URINARY APPARATUS

Introduction: Malformations of Kidneys and Ureters (lit. in appendix)

Embryological Introduction.—Uniformity of opinion has not been reached concerning the development of the kidneys. The idea in vogue for a long time was that the primordial kidney develops from the Wolffian duct at first as a solid bud. As the renal anlage gains in length it soon divides into the true kidney and the ureter. The formation of the kidney itself, according to the opinion of Toldt and Nagel, shared by O. Schultze and others, proceeds simultaneously, united with that of the ureter by a sprouting of all the renal tubules from the ureter. An opinion accepted at present is that the kidney has a double origin, *i.e.*, the anlage is discontinuous. (Lit. by Jageroos.) From the caudal segment of the primordial ureters, (Wolffian ducts), there grows a hollow bud, the ureter bud, becoming mushroom shaped, with a short pedicle the true ureter anlage, and a bulbous end which becomes the pelvis. From the latter only the ductus papillaris and collecting tubules develop, while the part corresponding to the cortex with its tubules and glomeruli develops from a separate "anlage," the renoblast of mesoblastic tissue. (Metanephrogenous tissue.) The latter covers, like a cap, the dichotomous branching buds which spring from the primitive ureter, *i.e.*, the primary pelvis. The urinary tubules then invade the ureteral branchings secondarily. (Details by Felix lit., Bonnet, Broman, Guillebeau, Rosenow, lit. a.o.) The close relationship borne by Müller's ducts to kidney development explains the coincident, not rare, occurence of both genital and renal malformations. (Spoken of under C.)

Congenital Absence of Kidney (Agenesia or Aplasia) and Atrophy (Hypoplasia). Bilateral absence (lit. by Coen and Schilling), or atrophy, or a combination of absence on one side and atrophy on the other, is very rare, and not compatible with post-uterine life. Hauch (lit.) reports a newborn child 45 cm. long, in which the kidneys, pelves and ureters were completely absent; there was oligohydramnion of only about 30 cc. Aplasia of one kidney is not so rare and in over one third of such cases, bilateral malformations are found in the female genitalia, and sometimes in the male. (Lit. by Ballowitz, Winter, Scheuer, Sternberg, Holzbach, Guizzetti a. Pariset, Weibel, Rosenthal, lit., Schillung lit.) The kidney present compensates by hyperplasia of both tubules and glomeruli, (Eckardt, Steinebach, lit.), and assumes the entire excretory function; its weight may correspond to that of two healthy kidneys. The acquired absence of a kidney after birth, on the other hand, leads to enlargement of the remaining kidney only by hypertrophy, the more marked the younger the individual. The solitary kidney becomes diseased relatively more frequently probably on account of the increased demands made upon it.

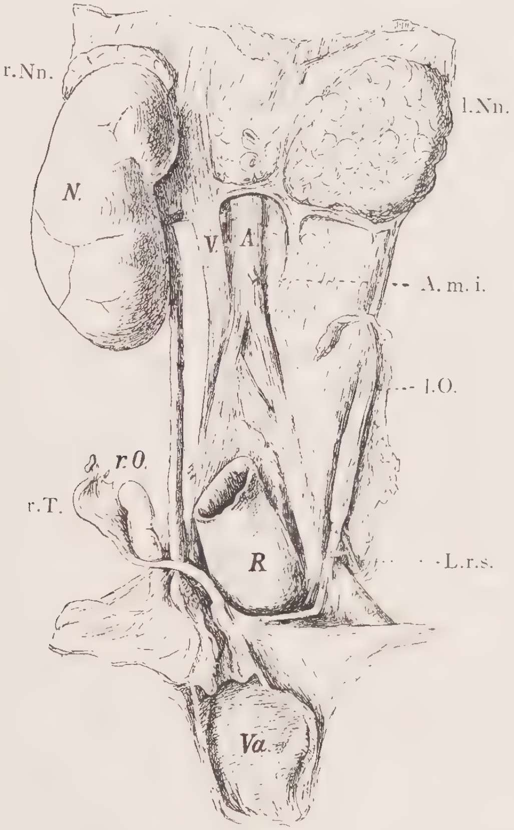

FIG. 669.—Left renal defect, uterus unicollis, 9 weeks old girl with congenital syphilis. N, r. kidney; r.Nn, r. adrenal; l.Nn, left adrenal with l. suprarenal vein; V, vena cava; A, aorta; A.m.i, inf. mesent. artery; r.O, r. ovary; l.O, l. ovary; r.T, r. tube; L.r.s, l. round ligam. in inguinal canal; R. rectum; Va, vagina; ¾ nat. size.

(Lit. by Th. Cohn.) The left kidney is absent more frequently than the right (Klebs), and twice as often in males. The corresponding ureter is also usually absent and the bladder has only one ureteral orifice. Rarely two ureters pass upwards from the bladder; that from the missing kidney ends in a cul-de-sac. In a thirteen year old boy the author saw the left ureter end blindly where the kidney should have been, but it was open to the probe from below, was distended, markedly thickened and aided in a diverticulum of the urinary bladder. Congenital unilateral renal atrophy (hypoplasia) is very rare; the rudimentary organ contains few or no tubules or glomeruli. In older individuals it is naturally difficult to distinguish congenital hypoplasia from acquired atrophy. (Motzfeld; lit. by Gruber a. Bing.)

> **Translator's Remarks.**—Pepper and Lucke report a case of fatal chronic nephritis in a fourteen year old girl with only one kidney and a history of scarlet fever (Arch. Int. Med. 27: 661: 1921). The presumption is that if such individuals had both kidneys, they would live longer.
>
> According to Arataki's data on rats, the formation of glomeruli is very active during the first thirty five days of life but continues until one hundred days at least (corresponding to about nine or ten years of human life). But the diameter of the glomeruli increased even to five hundred days. The diameter of the convoluted tubules did not increase from birth onward. Results found in the surviving kidney examined at various intervals after unilateral nephrectomy showed that enlargement is due mainly to hypertrophy of the glomerular unit systems, lengthening of the convoluted and collecting tubules, hyperplasia of the supporting tissue and hypertrophy and hyperplasia of the tubule lining cells (Am. J. Anat. 36: 399–450: 1926).

Fusion of Both Kidneys (Ren Concretus or Impar).—If the embryonic anlage of the kidneys are too close together, fusion may result, often accompanied by displacement (dystopy). The fusion is along the lower poles thus forming the horseshoe kidney. Keyes found it 16 times in 11,000 autopsies. The union may be fibrous and the kidneys in normal position, or the left kidney is pulled over towards the right, but frequently there is a connecting isthmus of parenchyma which eventually becoming the main part gives the impression that the fused kidneys are only one. The broader the parenchymatous bridge, the lower towards the pelvis is the position of the organ. The shape of fused kidneys varies; they are cylindrical, round, flattened, or composed of irregular nodules and lobes, (atypical form, see Carlack). The horseshoe type is usually open above, rarely below; or the kidneys are fused along their entire medial surfaces, (cake kidney), or one lies behind or above the other, etc. The pelves and ureters are situated anteriorly. Both pelves may be fused or separated into several sections outside the kidney. The horseshoe kidney is frequently subject to disease. (Adrian and Lichtenberg lit., Eisendrath.)

Anomalies in the number of vessels are two or three to one kidney; the arterial source is also varied, *e.g.*, arteries may come from just above the iliac bifurcation, or from one iliac artery; a branch may extend to the center of the horseshoe. The same is true of the veins, the pelves, the ureters, of which only one, or both, or two on both sides may be present, (good summary by Pohlmann; see Verocay and especially O. Meyer in relation to the vessels—with regard to multiple renal arteries in general, see Seldowitisih).

Congenital Displacement (Dystopy) of the Kidneys.—If the ureter anlage does not lengthen normally, a single kidney, frequently the left, or both fused together, may be situated far below the normal position, such as over the sacrum, or lower in the pelvis—primary pelvic kidney, (lit. by Brettschneider), even in the inguinal ring. The hilus of the misplaced kidney may be directed forwards or backwards; its ureter is short and not convoluted, in contradistinction to that in acquired renal displacement; it receives its arterial supply from the lower aorta or from one iliac artery though not always from that of the same side. The inferior mesenteric artery also frequently gives branches to the displaced kidney; the author saw it twice in five cases. The venous supply is likewise quite variable, (Anitschkow), but the vessel relations in general are secondary. (Thomas.) The corresponding adrenal is usually in its normal position. For the microscopic details in congenital ectopic kidneys, see Lejars and Rubens-Duval. These malpositions are sometimes coincident to mal-

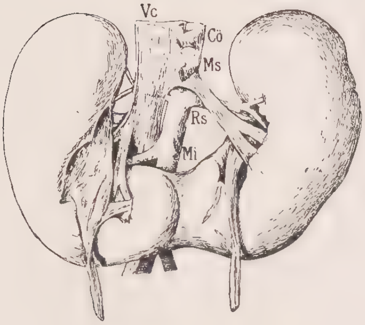

FIG. 670.

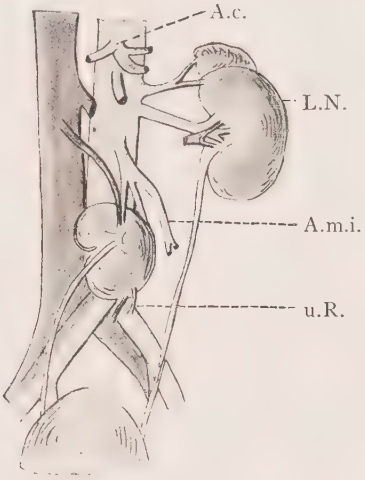

FIG. 671.

FIG. 670.—Typical horse-shoe kidney of man 28 years old. Abnormal relation of vessels; right, two renal arteries; left, one (Rs); celiac art. (Co); and sup. mes. (Ms). The lower r. renal artery lies at level of inf. mes. art. (Mi); course of veins also asymmetrical; Vc, vena cava. Below the isthmus of the horse-shoe kidney lies the bifurcation of the abdom. aorta into the iliac arteries; ⅓ nat. size.

FIG. 671.—Dystopia of r. kidney of man 45 years old. LN, l. kidney and adrenal; Ac, celiac art. (tripus Halleri), below this the sup. mes. art. At the r. kidney an upper art. is seen coming from a trunk which also gives off the inf. mes. art. (A.m.i.) and the r. int. spermat. art., u.R.; r. lower art. coming from the r. iliac art. The relations of veins are at once apparent.

formation of the female genitalia, (lit. Engstroem, Pepere, Weibel); malformations of the bowel are rarer. Renal dystopy may lead to diagnostic errors in the living, being mistaken for tumors of the ovaries, tubes, uterus, undescended testicle, etc., and may also act as an obstruction during labor.

Changes in the Shape of the Kidneys. Supernumerary Kidneys. So-called congenital lobulation depends on the persistence of fetal furrows which outline the renculi, or minute renal anlage. They vary in number and are developed by the metanephrotic tissue which in globular shell-form surrounds each collecting tubule system separating them more or less sharply from their neighbors. These deep surface furrows must not be mistaken for the scars of infarction. A perfectly even double division of a kidney, with two chief calices (ren duplicatus) is rare; there are separate parenchymatous regions, not always externally visible, double pelves usually asymetrical, and single or double ureters. The two separate main calices may also have a pelvis in common with one ureter, as the author saw in a man sixty-six years old. The following may serve for an explanation: double ureteral buds grow out of the primitive ureter; both primary pelves become surrounded by the metanephrogenous tissue which then results, as a rule, in one kidney, or a double kidney, (see above), with the double ureter. But if the separation of this tissue into two parts is complete, true supernumerary kidneys are formed (rare). (See Broman, and cases by Dixon, lit., and Mills.)

Malformations of the Renal Pelvis and Ureters.—We find reduplication or further separation of the pelvis when the calices are changed into fibrous tubes; at the same time, several separate ureters, or only one, may be present, (see Wossidlo). Double ureter may be uni- or bilateral, and can be explained by the appearance of two ureteral buds, and two ureters growing from the wall of the primary urinary duct. This doubling may be complete; two separate ureters from one kidney descend side by side, and cross, usually at their lower end. They may enter the bladder separately, one behind the other, one above the other, rarely side by side, in which case the upper one on entering is always lower, *i.e.*, caudal, or medial, or lower and medial from the entrance of the lower ureter. The ureter may be in duplicate above, or only one of the double ureters reaches the bladder, while the other ends in some abnormal situation. (For details, see R. Meyer, lit. Wimmer, lit. and Handl, lit.) The opening of a ureter in an abnormal place, may occur also with a single ureter, and is usually into the urethra directly beyond the bladder, but occasionally into the seminal vesicles, on the colliculus seminalis, into the uterus or vagina. Stenosis and atresia of a ureter or a part of the pelvis may be caused by a blind ending (aplasia), or developmental inhibition of a section, and possibly also from intrauterine inflammation. The stenosis may be uni- or bilateral, annular or linear. Even congenital strictures may lead to complete atresia. Hydronephrosis is the result, and, eventually, hydroureter; or if the condition develops very early, total functional atrophy of the kidney. If a ureter ends blindly at its vesical end, when there is also an open ureter on the same side, or if the vesical orifice of one, or, as the author saw, of both ureters, narrows down to an exceedingly fine opening, (phimosis of ureters), the vesical end of the ureter covered with vesical mucosa bulges into the urinary bladder like a bubble or cyst; (uretrocele vesicalis) (Bostroem, Stoeckel, English, lit., Cohn, lit., Koenig, Kapsammer, Regner, Blum, v. Franque, Pleschner, lit.). Among other things, it may intermittently prevent the outflow of urine. Hematuria consequent to hyperemia of the cyst is not rare. The cyst, in size from a cherry stone to a fig may also rest on the vesical orifice (see Geipel and Wollenberg). In other cases, for instance that of Hibler, it may actually appear between the labia. This cystic dilatation must be differentiated from eversion or prolapsus of the lower end of the ureters, (lit. Blum). Valve formation by mucosa folds, kinking, or torsions of the ureter, often easily traced to renal ptosis or hypermobility may cause hydronephroses (see Bazy). If the ureter is inserted into the renal pelvis at a very acute angle, and the pelvis is filled, the ureter may be laterally compressed and this may be followed by hydronephrosis. It happens on one side, but more frequently on both sides. It may also occur, as seen by the author, in cases of double pelvis and double ureter, to one division of a double pelvis, when the portion with its ureter inserted low down is not enlarged. According to Handl, congenital vesical diverticuli at the ureteral orifices must be considered as abnormally enlarged remnants of the primitive ureters (synonymous with Wolffian ducts). Very rarely there occur multiple diverticuli of the ureter with blind ends. (Pepere.)

Normally, in the fetus and the newborn, there are two spindle-shaped dilatations of the ureter (lit. Seitz).

KIDNEYS

(See Disse, Peter, Metzner, O. Schultze, Susuki, Fahr, v. Moellendorf in reference to the structure and function of the normal kidney.)

The urinary tubule system with its glomerulus, together called the nephron, is divided into the following parts: capsule epithelium, proximal convoluted tubules, called by Peter "chief substance;" the loop of Henle with its descending, narrow, transparent, and its ascending thick, opaque limbs, the middle part, lined by flat cells which closely surround the capsule of the glomerulus; the distal convoluted tubules; and the collecting tubule which empties with others into one of the larger papillary ducts. The proximal convoluted tubules are distinguished from all other parts by a brush-edge. According to function, it is convenient to differentiate secreting convoluted tubules, absorbing Henle's loops, (middle parts), excreting collecting tubules, and ductus papillaris. (See Aschoff.) It is still a matter of dispute whether most of the urine is filtered through the glomerulus, (lit. by Aschoff) or is secreted. (Lichtwitz.) (See question of reabsorption or concentration of urine in the intermediate part by Jacobi, Lichtwitz, etc.)

The normal weight of both kidneys in adult males is 250–300 grams; in females about 25 gms. less. Its size is 11–12 cm. long, 5–6 cm. wide, and 3–4 cm. thick; in newborn males both kidneys weigh about 25 gms., in females 20 gms. They are usually of equal size, but the author has seen the left twice as large the right.

Post mortem changes are important especially in considering microscopic findings; they occur quite quickly in the epithelium, especially of the convoluted tubules; the cells appear granular, and the rods, as far as they are perceptible, become diffusely stained with iron hematoxylin and frequently change into granules. The brush edge resists autolytic processes much longer. Myelin droplets frequently break through the brush edge from the protoplasm into the lumen of the tubules. The epithelium of the decending loops is more resistant than that of the straight tubules. The most important marks of differentiation are: the kind and degree of post mortem change in the different parts of the tubule system are everywhere the same, thus differing from the pathologic forms of localized, and more or less marked, changes. With increasing autolysis, the brush edge disintegrates into the picture of coagulation, the nucleus cannot be stained, and the cells separate from each other. Many artefacts are caused by unsuitable fixing solutions, especially when not isotonic. Recognition of the endothelial cells becomes difficult, but the glomeruli resist longer and, generally speaking, are well preserved, even after 24 hours. All of these considerations may be modified in cases in which autolysis of the body takes place quickly, as in sepsis, etc. (see Policard and Garnier, Aschoff, Oka).

Acquired Displacements (Floating Kidney) (Ren Mobilis, Nephroptosis)

Floating kidney is an abnormal and probably acquired mobility of the organ of varying extent. It is a quite common condition, ten times more frequent on the right side than the left, and occurs much oftener in females especially of advanced age. The kidney becomes (*a*), abnormally mobile in its relaxed perirenal connective tissue, but still in its normal place, or (*b*) its long axis becomes more or less horizontal and the entire organ lies below its normal situation, or (*c*) a more advanced condition, the kidney slips forward and downward into the iliac fossa being quite freely movable with the relaxed peritoneum and subperitoneal cellular tissue. As a rule the colon is also ptosed. In (*c*) it is permissible to speak of "wandering" kidney, which is revealed on standing, and replaced on assuming the horizontal position. The organ usually describes the arc of a circle around the fixed but stretched renal vessels; the pelvis naturally occupies a superior position. The floating kidney may become fixed in an abnormal situation. If the kidney is low, the distance traversed by the ureter, normally 25–30 cm., is naturally decreased and it becomes convoluted. This may lead to kinking and subsequent hydronephrosis, (experiments of Tuffier, Hildebrand and Haga).

Etiology.—Floating kidney is caused by pressure on the liver in tight lacing, by tumors of the liver, etc.; from laxity of the capsule and peritoneum, as after pregnancy; from disappearance of the fatty capsule and senile relaxation of tissues from advancing age, but especially from enteroptosis, in which the usually heavy liver forces the right kidney downward. Increase in weight of the kidney may at times be responsible, as in tumors, cysts, hydronephrosis, etc. Trauma such as contusions, etc. may also be a direct or indirect cause (lit. by Schlagenhaufer).

Clinical symptoms occur in relatively few; most cases are latent. At times disturbances in secretion of urine appear as in hydronephrosis (p. 1403). The clinical manifestations of so-called incarceration are probably due in most cases to torsion of the ureters, the renal nerves, and vessels. Diagnostic errors may be made in the case of a liver with a marked lacing furrow, *i.e.*, a partly separated reniform lower end of the right lobe; fecal masses in the ascending colon, gall bladder enlargement, floating spleen, pyloric tumors, etc. (Surgical fixation of a floating kidney is called nephropexy; lit. by Tichy.)

Circulatory Disturbances

Congestion, Acute Hyperemia.—Acute hyperemia accompanies acute inflammations, and is caused by increased functional demands, as in a kidney that is compensatory for another, and, therefore, hypertrophic. It may also be caused by increased labor of the left heart. The kidney is usually enlarged, elastic, and may be diffuse or spotted red in color.

Venous, Passive Hyperemia.—Passive hyperemia is caused by impeded outflow of blood, as in general passive congestion due to the cardiac insufficiency of cardiac and pulmonary lesions especially disturbances of compensation. In other cases, stasis is caused by local conditions and these lead to the most severe grades. Among local causes are: compression of a vein, due to increased abdominal pressure, pregnancy, tumors, etc., occlusion by thrombosis, either blood or tumor, of one or both renal veins or their branches, or of the vena cava, above the entrance of the renal veins. A tumor thrombus, might be caused by the invasion of a renal tumor into a renal vein; a blood thrombus may be marasmic in cardiac weakness, or from circulatory disturbances in the kidneys themselves, as in amyloid disease, etc. Thrombi may form in the vena cava or in the left spermatic vein and be carried retrograde into the renal vein, or an embolus might be carried in a retrograde direction, (see page 169) or, finally, the thrombus may be of inflammatory origin as in pyelonephritis.

Results following obstruction of the renal veins: If complete, sudden or in a short time, the marked swelling of the kidney is due to retention of an immense amount of blood. Edema and hemorrhage occur not only in the interstitial tissue but also from the glomeruli into the tubules. If the obstruction is not relieved there follow cloudy swelling and fatty degeneration in about 12 hours, and finally complete necrosis, all of which changes are more marked in the medulla than in the cortex. At first the kidney is enlarged, thickened, soft and blackish-red; the urine shows blood, epithelial casts and cylindroids. Experimentally, (Buchwald and Litten), six days after ligation of the renal veins, progressive diminution in size takes place from disintegration of the epithelium, while the resistant glomeruli move closer together. The experimental animals remain alive up to 8 weeks by the development of a collateral circulation. If thrombosis is slow, the collaterals carry part of the blood to the phrenic, suprarenal and lumbar veins, also to the azygos and the hemiazygos veins. Thrombosis is occasionally seen in children, sometimes extending to the smaller branches with or without hemorrhagic infarction. In the latter case the kidney becomes very large and dark red, with medulla almost black and the pelvic mucosa in marked contrast by its pallor. This is chiefly in marasmic newborn children or sucklings, (Beckmann), which die with anuria, (urinary bladder empty), and spasms (uremia), at times also in exhausting diarrheas; there may occur coincident marasmic thrombosis of the brain sinuses, (see there), or in the veins of the thighs.

Generalized chronic passive congestion leads to the common congested kidney which is seen most frequently during the stage of so-called cyanotic induration.

Macroscopically, the kidney is enlarged sometimes by ⅓ of its size, and is very hard. The capsule is smooth and strips easily. On its surface, the stellate veins, are injected and bluish-red, even the most minute branches. On section, the cortex is bluish-gray to bluish-red. The glomeruli may be distinctly visible as red dots. The medulla is sharply differentiated by its darker color, especially at the base of the pyramids; the tint is bluish-red to blue-black, and striae of dark red color correspond to the arrangement of the vasa recti. The remarkable hardness of the kidney is due partly to the extensive filling of veins and capillaries, including the enlarged glomeruli, partly to simple hyperplastic processes consisting of thickenings and sclerosis of the venous walls and capillaries, and to a less degree to the interstitial connective tissue which becomes fibrous and glassy, especially in the medulla. The epithelium of the urinary tubules shows mild fatty degeneration, but in more advanced cases the cortex is yellow in spots or homogeneous. This is the chronic "fatty kidney of cardiac disease."

Since a mild degree of icterus is not rare under these conditions, the yellow color becomes more pronounced.

In contradiction to this marked fatty change, (sudan stain!), are the apparent firm consistency and smooth section surface of the kidney, but this is explained by the coincident tense congestion and induration.

After suitable fixation, (alcohol, formalin,) granular proteins can be demonstrated in many glomeruli and urinary tubules. Other tubules, especially those in the medulla, contain hyalin, colorless casts. Erythrocytes may also be present here and there in the connective tissue, in the capsular spaces, and in the tubules.

The blood pigment coming from red blood cells disintegrating in the tissue can be recognized as yellow, brown, granular or crystalline masses, especially in Henle's loops, or in the epithelium of the convoluted tubules. Sometimes it is present in sufficient quantity to cause a gross brownish discoloration of the medulla.

The urine from the congested kidney is decreased in amount and darker; instead of 1500–2000 ccm. only 500–300 ccm. are secreted daily; (Eichhorst); it is more concentrated, its spec. gravity is 1025–1030; (Senator); there is a heavy sediment of pigments, brick dust, urates, etc., easily dissolved by heating. Albumen is present, usually in small quantities, (1–2%). It contains hyalin casts. The decrease in quantity as well as the presence of albumen are explained by the reduction in the rate of blood flow in the glomeruli, as well as by the decrease of general blood pressure due to weakened heart action.

To this cyanotic induration, a cyanotic atrophy may be added,—the contracted kidney of passive congestion. The organ decreases in size and may show numerous small indentations on its surface where the capsule is adherent. The surface thus becomes nodular. It is differentiated from other contracted kidneys by its cyanotic color. The medullary cones are smaller, and consequently the pelvis is somewhat enlarged.

The pressure exerted by the hyperplastic interstitial tissue leads to atrophy of scattered urinary tubules and glomeruli. According to Schmaus and Horn, veins as well as arteries, in the former the adventitia, in the latter also the intima, are markedly thickened, and the interstitial tissue is considerably increased by a homogeneous fibrous-like substance.

Round cell infiltration especially around the veins, is often prominent. (Lit. by Oertel.)

Anemia (Ischemia) of the Kidney.—We shall discuss the special phenomena of general anemia, or the lessening of blood supply from local factors, (oligemia), as well as temporary interruption of the blood supply. The highest degree of acute anemia is seen in death from exsanguination; the kidney is clay-colored, but its firm consistency and absence of cloudiness prevent it from being mistaken for fatty degeneration. Anemia also results from occlusion of the renal artery (see below), or from rupture by trauma. The result is necrosis. In general chronic anemias such as chlorosis, carcinoma, and especially pernicious anemia, the fatty degeneration of the epithelium, especially of the convoluted tubules makes the consistency soft and the color pale yellow.

If the kidney receives an insufficient supply of arterial blood as, for instance, in the vessel spasm, of asphyxia, tetanus, strychnine poisoning, lead colic, and hysteria, or reflexly from irritation of a kidney or its ureter by a calculus etc., or indeed at times from only peripheral irritation, the urine is quantitatively diminished in amount and contains albumen. Even complete anuria may be established. According to Cohnheim, the epithelium of the glomeruli suffers in anemia and becomes permeable to albumen.

Coagulation necrosis of the uriniferous tubules can occur after a relatively short cessation of blood supply or with marked lowering of blood pressure (p. 1304).

It was formerly thought that the epithelial necrosis of the kidneys in cholera was due to the marked fall in blood pressure (ischemia), (Griesinger, Leyden a. o.), but Eug. Frankel and Simmonds viewed these changes as toxic, while others, (Furbringer), considered it an effect of both ischemia and cholera toxin. Similar changes occur in bichloride of mercury poisoning and occasionally in pertussis, (Mircoli), after influenza, (Beneke), and as an after effect of chloroform anesthesia (Fraenkel). In eclampsia, the occasional extensive microscopic necrobioses of the epithelium of the cortex were charged to generalized arterial spasm, (Schmorl, Beneke); it appears more logical, however, to think of a toxic process, but not as in the former view of the primary cause of eclampsia in the kidneys. According to v. Winkel, the "kidney of pregnancy"[1] is found in about 2% of pregnant women, usually primipara, in the second half of pregnancy.

Others speak of pregnancy nephritis (lit. by Seitz), but according to v. Jaschke, (lit.), it is a typical nephrosis, characterized by albuminuria, edema, cylindruria and absence of hematuria; there is injury, not only to the tubular parts but also to the vessels, the latter accounting for the edema. According to Schlayer, however, the injury to the vessels is functional and not evident morphologically. On the other hand, Lohlein found a peculiar thickening of the capillary walls which he is inclined to consider primary and on which depend the degenerative tubular changes. If it is considered that others accept the term "nephrosis" strictly in the sense of tubular or epithelial degeneration, speaking especially of a tubular epithelium nephrosis, while still others speak of nephropathia gravidarum, etc., the simple designation given above gains in value as helping a uniform nomenclature (see p. 1318). Besides mild degenerative processes in the epithelium of the tubules, fatty degeneration of the glomerular epithelium has been described, and this is said to have ischemia as an immediate cause by pressure or reflexes from the gravid uterus. Others believe, probably with more justification, that the cause is a toxin of unknown composition but elaborated during pregnancy and possibly originating from the fetus (?). The functional changes are usually slight, and as a rule complete recovery takes place soon after delivery. (Lit. by Pollak, v. Jaschke.)

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[1] The designations such as cholera kidney, sublimate kidney, eclampsia kidney etc., tell us that the changes in the kidney were caused by these different factors—an advantageous viewpoint because it does not prejudice with regard to the modus operandi. (See Lichtwitz, Kautzky.)

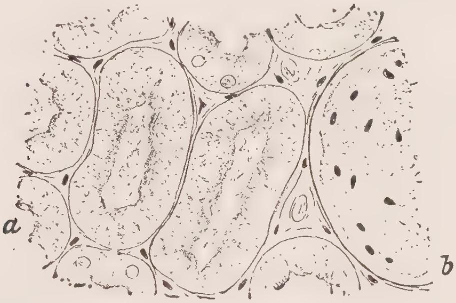


FIG. 672.—From an anemic infarct of kidney; a, necrotic epthelium of canaliculi which contain granular coagula; b, piece of swollen necrotic glomerulus with sparse nuclei. The kidney stroma still takes nuclear stains (living). (Medium magn.)

Occlusion of the Renal Artery and Its Branches. The Formation of Infarcts.—The main trunk of the renal artery may be occluded suddenly, by an embolus as in endocarditis, or, rarely, by a thrombus gradually forming in situ and following traumatism (tearing). If the vessel is completely occluded, the kidney at first appears pale, uniformly yellow-green or yellowish-white, as though boiled, and in time shrinks to a body the size of a bean.

According to the investigations of Litten, ligation of the renal artery does not cause anemia, but hyperemia, most noticeable at the border line between the medulla and the cortex, where the pressure in the collaterals is weakest and where there is the most stagnation of blood. These collaterals are carried in the ureters and in the renal capsule. (See Liek in reference to the collateral circulation of the kidney.) If the ureter is ligated and the capsule stripped at the same time, no hyperemia develops; if the ligature remains, there is complete death of all the tissue by simple or direct necrosis. If the ligature is applied for only a short time, (1 to 2 hours), the most sensitive parts of the organ perish, *i.e.*, the epithelium of the convoluted tubules in a coagulation necrosis (Cohnheim, Weigert), or necrobiosis, or indirect necrosis. This form occurs especially if injured living tissue dies while it contains coagulable substances such as blood or

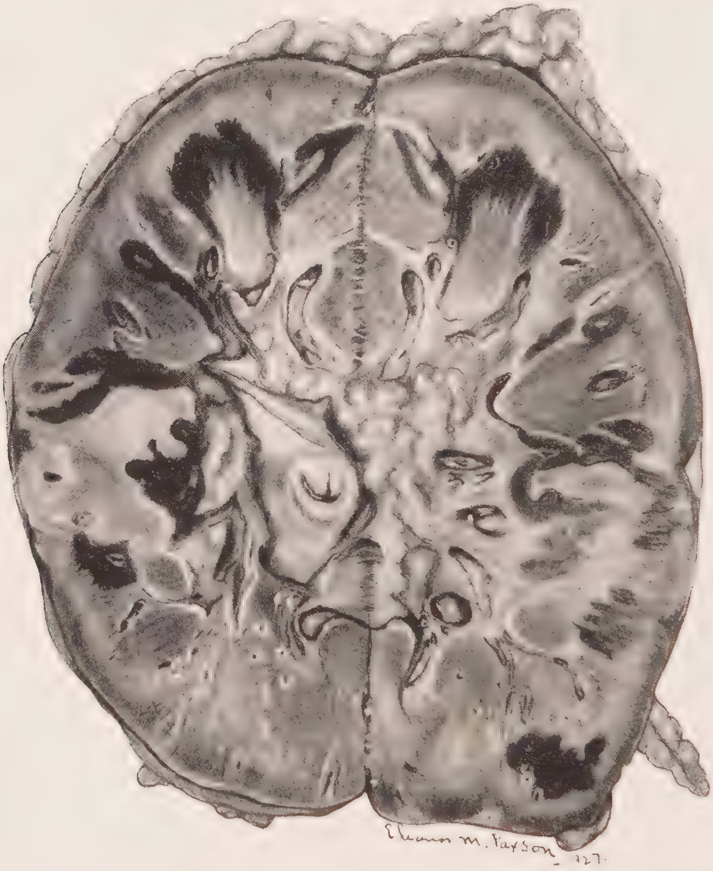


FIG. 673.—Infarction of entire kidney. This occurred in a patient 38 years old who had bilateral ulcerative phthisis for five years. She was seized suddenly with severe pain in the right kidney region with shock and great prostration. She died about twenty-four hours later. At autopsy a firm but crumbly thrombus was found in the right renal artery and a softer thrombus in the right renal vein. The entire kidney was slightly swollen, cloudy, its finer landmarks extinguished and small hemorrhages present in the cortex with deep congestion of the bases of the pyramids. There was no obvious source of embolism found in any part of the body examined and the case was possibly one of autochthonous thrombosis in a patient severely ill with pulmonary tuberculosis. L. H. #191.

fibrinogen-containing lymph. The epithelium becomes a granular, anuclear mass; between the cells and within the lumena of the urinary tubules are thread-like and hyalin coagula. Afterwards, the necrotic epithelium may take up large amounts of calcium salts. The ischemic degenerated cells of the convoluted tubules, and the broad parts of Henle's loops, lose their granules. (C. Hirsch.) See Turk, (recent lit.), in reference to degeneration of renal cells in obstruction of the circulation for longer periods.

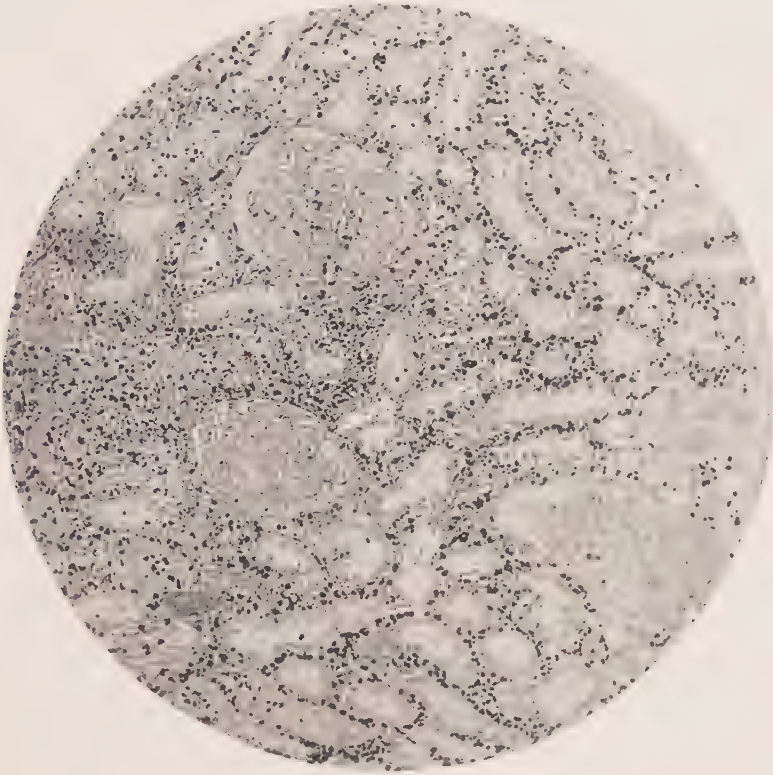


FIG. 674.—Section of the infarcted kidney of Figure 673. There are necrosis of all parts, karyorrhexis of nuclei but no hemorrhage in this particular section. × 110. L. H. #191.

More frequently only isolated branches of the artery are occluded by embolism or thrombosis.

Thrombosis may occur subsequent to atheroma or trauma of the renal artery, and in general infections; thus Moenkeberg observed thrombosis of both renal arteries in a case of erysipelas of the thigh. Tuberculous arteritis may also cause obstruction.

Not rarely an embolic obstruction becomes complete through secondary thrombosis, or a soft thrombus in a large vessel breaks into numerous emboli which are scattered through its branches. The kidneys are organs of predilection for embolism and since the left renal artery leaves the aorta at more than a right angle, it is favored over the right. The emboli themselves may be torn off thrombus material as in endocarditis, especially mitral, atheroma, etc. The portion of the kidney supplied by the obstructed vessel undergoes necrosis.

After even a short time, (hours), the epithelium, still recognizable in its outline, is necrotic, the nuclei cannot be stained and the cells appear as lusterless, transparent clotted masses. Here and there fatty degeneration is seen. The connective tissue and the glomeruli remain well outlined and die only after a longer period. The parts containing tissue lymph undergo coagulation necrosis, are somewhat more voluminous, and changed into a homogeneous, or grumous, or stringy, substance. The chromatin of the nuclei is completely lost. Simple necrosis takes place in the center of larger foci, (Litten); where the solvent juices are absent, necrotic nuclei may still contain chromatin disintegrated into fragments and granules. (Karyorrhexis.) Weigert's fibrin stain may demonstrate fibrin coagula in the capillaries between the dying uriniferous tubules,

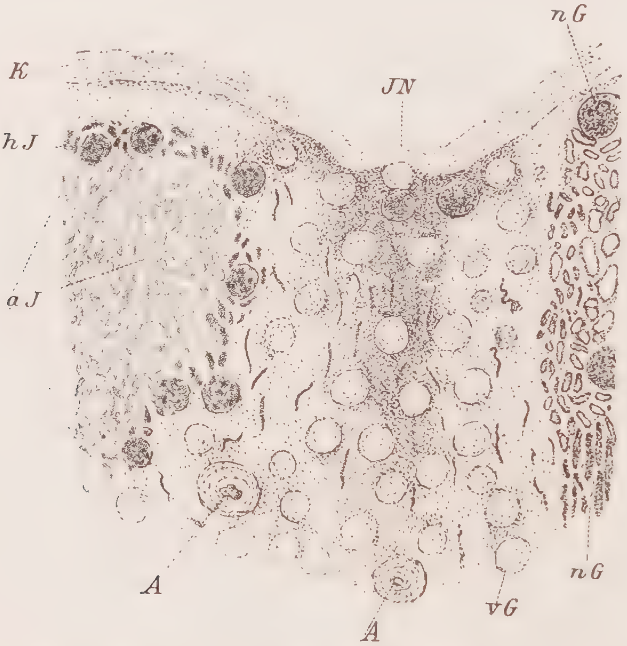


Fig. 675.—Anemic infarct (aJ) with hemorrhagic infarcted zone (hJ). Alongside (JN) old infarction scar with pulling in of surface; K, thickened capsule. In the fibrous-cellular tissue of the scar are numerous atrophic and hyalin dead glomeruli (vG) and in between here and there rudimentary tubules; much brown pigment within the scar. In transition areas to normal tissue of kidney (nG) small, narrow, newly-formed urinary tubules; A, thickened, recanalized arteries. (Low power.)

especially along the outer edges of the infarct. (See lit. by Brault and Courcoux.)

In reference to hemorrhagic infarction of the medulla in the newborn, said to be caused by toxic injury, paralysis, excessive dilatation, or diapedesis through capillary walls, and leading to compression and destruction of the tubules through interstitial hemorrhage, see Oppenheim.

Collateral hyperemia and more or less extensive hemorrhage appear in the vicinity of the infarcted area. On macroscopic section, there is a right-angled or wedge-shaped structure (anemic infarct) within the obstructed region, generally clay-colored, pale, without lustre or moisture, opaque, of cooked appearance, firm consistency, and surrounded by a red zone or red spots. Not rarely there is also a sulphur-yellow line between the red zone and the grayish-yellow clay colored focus.

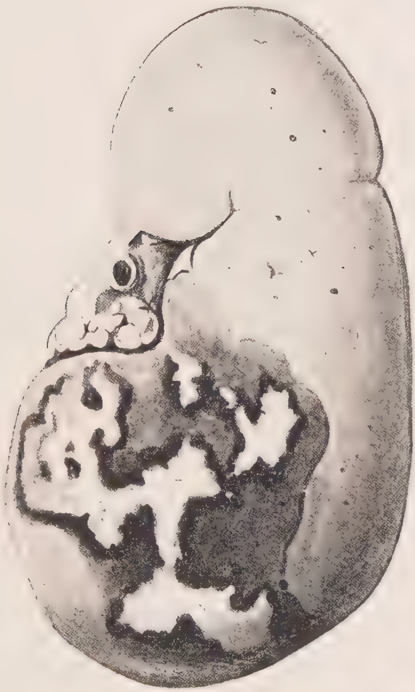


Fig. 676.—Renal infarct. (anemic hemorrhagic); man 61 years old with mitral stenosis, hypertrophy and dilatation of heart; ⅞ nat. size.

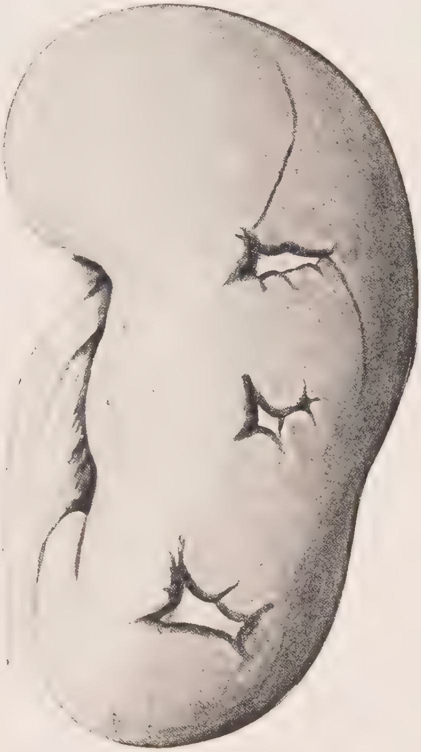


Fig. 677.—Anemic infarct of kidney with beginning cicatricial contraction; man 20 years old with recurrent mitral and aortic endocarditis; ¾ nat. size.

It is not advisable to say "anemic sequestrum" in place of "anemic infarct" or wedge; it becomes analogous to a bone sequestrum only if separated from its surroundings which never happens in this case.

In the tissue surrounding the infarct, the epithelial cells with well-stained nuclei contain fat droplets, but since the nutrition is supplied by the blood and fluid currents of the vicinity, the fat remains, for obviously the metabolism is sluggish. The same condition occurs in the connective tissue further removed from the edge, and fat droplets collect between necrotic tubules. The edges show marked vascular dilatation and even hemorrhage; they also participate in the regenerative processes (p. 1309). Occasionally diffuse calcification takes place in the border zone.

If the infarct is wedge shaped, the apex is directed toward the pelvis and ends most frequently at the junction of medulla and cortex. The base extends to the surface and may be elevated like a flattened sphere. If the base of the wedge stops short of the surface, it means that the subcapsular parts have been bathed in blood from the collateral capsular arteries and have thus escaped necrosis; these collaterals must open at the very beginning. If there are several infarcts close together, the surface is map-like and marbled, and the infarcted area is distinctly larger than the normal.

Fate of the Infarct.—As the infarct is gradually dissolved (autolysis) and absorbed, it diminishes in size and becomes dry and hard, after which the surrounding tissue shows reactive infiltration and tissue growth. The interstitial tissue around the edges of the infarct is filled with migrated leucocytes, which later disappear through fatty degeneration and karyorrhexis. Granulation tissue penetrates the infarct as the necrotic tissue disappears and any connective tissue, *e.g.*, of vessels in the infarct itself, which escaped necrosis, participates in the organization process. There is also perhaps a weak hyperplasia of epithelium (mitoses!) proceeding from the edges. As the young connective tissue becomes a contracting cicatrix, the site of the infarct is pulled inward, perhaps quite deep and funnel-shaped. Numerous and larger scars cause lobulation, shrinking, and nodular malformation of the organ (embolic contracted kidney).

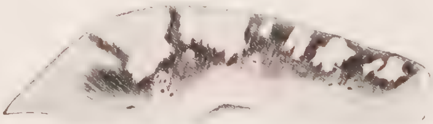


FIG. 678.—Section through renal infarction. The small pale infarcts do not reach to the cortex. Anemic infarcts surrounded by broad red zones; nat. size.

Microscopically, small amounts of necrotic material usually remain in the wedge-shaped scar, and a more or less nucleated connective tissue contains numerous necrotic glomeruli. Rudimentary uriniferous tubules are found in the peripheral parts of the scar, and occasionally also within it. Their epithelial cells are small, low, and stain intensively. (Fig. 675.) They are analogous to the proliferation of bile ducts in cirrhosis of the liver, and should be considered both as old atrophic, and newly regenerated tubules. (Mitoses!) (Thorel.) They are also encountered in other conditions in which renal tissue has broken down. As a phase of these attempts at regeneration, giant cell-like hypertrophies of epithelium are also seen. (Roessle.) The brown or yellow pigment in the scars is derived from the imbibed extravasated blood. At the apex of the scar is a closed or recanalized artery and even in the scar itself, larger sclerosed arterial branches may be preserved. Sometimes a slight lime deposit is present.

Langemak, in experimental investigations, came to quite different conclusions in reference to the formation of the scar, inasmuch as he considers it due only to the induration of remaining connective tissue, and not to penetration from adjacent structures. Lange partially supports this view.

Under What Conditions is a Hemorrhagic Infarct Produced?—While as a rule the occlusion of a branch of the renal artery results in an anemic infarct as just described, there also occur in the kidney, although less frequently, small hemorrhagic infarcts. At first purely anemic, they are soon flooded with blood, of course, non-circulating, from collaterals in the neighborhood. The blood escapes by diapedesis and remains in the tissue, although some may escape into the uriniferous tubules and so into the urine.

If there is a source of emboli, if sudden pain in the renal region occurs with hematuria, and if these symptoms disappear soon afterwards, "hemorrhagic infarct" may be diagnosed clinically (Leube).

Pressure in the collaterals forces blood for only a short distance into the dead tissue; beyond this the resistance is too great. For this reason smaller infarcts and the edges of larger areas are hemorrhagic, while large infarcts are essentially anemic, unless the blood pressure, is abnormally high. The hemorrhagic area is therefore usually a red edge around a larger pale infarct, while a red infarct is a deep red wedge which subsequently becomes brown-red, brownish-yellow, yellow, clay-colored and finally colorless. It was formerly thought that every pale infarct had experienced the same progression.

Microscopically the decolorized hemorrhagic infarct shows large quantities of old blood pigment; it retrogresses by fatty degeneration and the scars of hemorrhagic infarcts show brown pigmentation.

Absence of Infarction.—Not every embolism of the renal artery is followed by infarction. Apart from the facts that occlusion of the renal artery is followed only by necrosis, and that many emboli do not totally occlude, and that the introduction of very small emboli does not result in necrosis if the area involved is small and in the subcapsular region, the capsular artery may promptly supply sufficient circulation.

Very peculiar conditions are presented by rare cases of symmetrical total necrosis of the cortex in eclampsia which lead to death with uremic symptoms. Immense, firm, cloudy, yellowish, red-rimmed necroses are infarctions involving more or less completely the whole cortex with thrombosis of intrarenal arterial, venous, and capillary branches in which Herzog found hyalin fibrin thrombi. These necroses have been explained in various ways. Schmorl and Beneke consider general arterial spasm responsible for the extensive microscopic necrobioses of renal cortical epithelium in pregnant women who succumb to eclampsia; Jardine and Teacher assume that spastic contraction of small vessels with thrombosis is responsible also for the macroscopic cortical necroses. Zansig, (Beneke's Institute), described "ischemic total necrosis of the cortex of both kidneys" after injections of camphor; he explains the escape of the medulla by assuming that vessel spasm ischemia does not injure these parts so severely because they are less sensitive to oxygen deficiency. But others believe a toxic cause produces both the liver and kidney necrosis and vessel thrombosis. (Lit. by Jardine and Kennedy, Herzog, Rolleston, Schuppel.) Stoeckenius saw almost complete bilateral cortical necrosis in diphtheria; (acute toxic thrombosis).

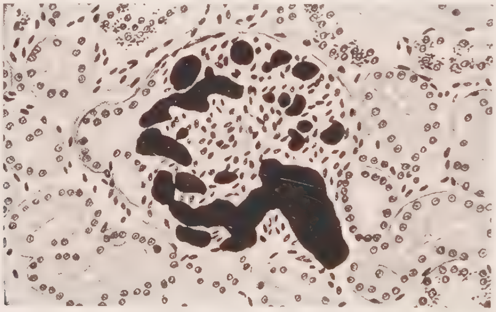


FIG. 679.—Fat embolus of a glomerulus, from a case of multiple traumatic bone fractures. Fat stained brown-black by osmic acid. (Medium magn.)

Fat Embolism.—Fat is found frequently in the capillaries, especially those of the glomeruli under the conditions described on pages 386 and 387. Fat may also appear in the urine with albumen as the expression of renal injury; (fat reactions on page 52).

Renal Atrophy

Senile atrophy with decrease in size of both kidneys in all dimensions is the purest form of simple atrophy and is part of the general involution of advanced age. The color is usually dark, reddish brown. The process may be quite uniform and the cortical surface is smooth or very finely granular, or it may be focal with pitted surface indentations deeper red in color than the surroundings. The weight of the kidneys may fall to below one-half of the normal.

Not rarely, minute cysts are seen, some on the surface, some in the parenchyma; their contents are water clear, or yellowish, thin, or jelly-like, and not rarely calcareous.

The fatty capsule and the fat tissue of the pelvis may be markedly developed. (Capsular lipoma.) In an obese man 80 years of age with kidneys weighing 135 gms., the author saw a capsular lipoma weighing 745 gms. The fibrous capsule usually strips easily. Such atrophies are essentially dependent on diminution in size of the epithelium of the convoluted and straight tubules; it is lower, the nuclei smaller and more intensely stained, the tubules narrower, while here and there the atrophy progresses until whole tubules disappear following obliteration of the glomerulus belonging to that system. The glomeruli, smaller or totally obliterated by hyalin degeneration, are crowded together; as the atrophic changes continue their loops gradually receive less and less blood; the endothelium and epithelium, are destroyed, individual capillaries become more and more glassy and hyalinized until they fuse with the hyalin connective tissue of the capsule into a shrunken clump.

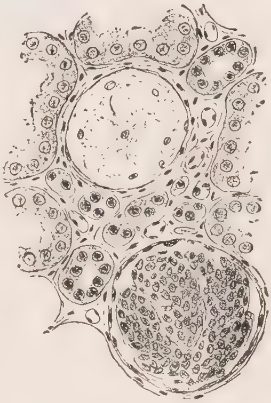


FIG. 680.—Senile atrophy of kidney. Above, an atrophic obliterated glomerulus; a normal one below; between are atrophic urinary tubules. In the periphery of illustr. are parts of normal convoluted tubules. (Medium magn.)

There is a question as to whether glomerular atrophy may follow primary destruction of the tubules; this is not generally accepted but Lohlein thinks it can probably occur because of the proved analogous sequence in hydronephrotic shrinking. He later described such a case of pure (?) atrophy, although even in his case the relations might have been vice versa. (See p. 1313.)

The capsule undergoes slight thickening and the interstitial connective tissue is slightly increased (compensatory) around atrophic tubules and glomeruli. But small cell infiltration, especially around the intermediate parts, does not belong to pure senile atrophy. Both the epithelium of the intermediate parts and loops, and the interstitial substance contain a yellowish-brown, non-iron reacting finely granular, fat-containing pigment, increasing with age (lit. Schreyer). It gives the senile kidney its brownish color. According to Prym, senile atrophy also shows a spreading of the medullary rays by perivascular fat deposit; (see Furno—the senile atrophic kidney).

Other forms of simple atrophy are arteriosclerotic, and will be discussed later. Pressure atrophy may be called simple atrophy when it occurs from urinary retention, (comp. hydronephrosis), or tumors or cysts in the vicinity. In these cases also, the uriniferous tubules disappear before the glomeruli. Thus obstruction of the collecting tubules in any area leads to atrophy (inactivity) of the entire tubule system above. With deeply seated tumors we sometimes find sharply demarcated wedge shaped infarction-like scars in the adjacent renal substance. (Beneke.) Finally, if we use the word atrophy in a broader sense, every diminution of the organ and all inflammatory contracting processes with disappearance of parenchyma are atrophies whether primary or secondary in the kidneys.

Arteriosclerotic Renal Atrophy.—Arteriosclerosis of the renal arteries and their larger branches is but a part of general arteriosclerosis and is consequently, as a rule, a disease of advanced age. The resulting changes are closely related to senile atrophy, and are actually considered by many as only a special form of this condition. Through a very slowly progressing thickening of the walls, especially the intima, the lumen of the vessel is narrowed or completely occluded. As the glomeruli are gradually deprived of their blood supply, they undergo atrophy followed by secondary atrophy of the tubules with gradual diminution in size of the epithelium. Finally the latter disappears completely and the tubules are obliterated. The slow progress and the involvement of focal regions

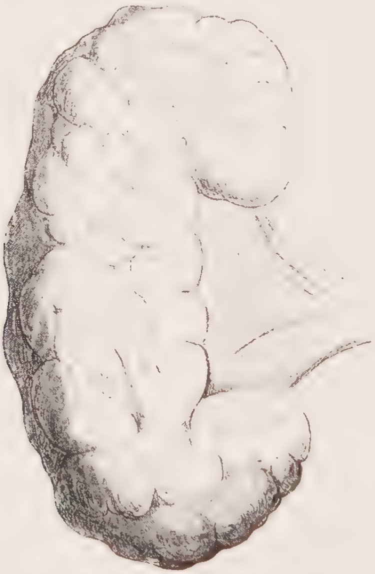


FIG. 681.—Arteriosclerotic contracted kidney, very marked, roughly nodular atrophy of kidney in general arteriosclerosis; participation by many branches of renal arteries; nat. size.

supplied by a particular arteriosclerotic vessel, gives this kidney a very characteristic nodular appearance. Only in places is the capsule more or less adherent; on stripping, there appear flat, very irregular depressions of the surface, perhaps of considerable size, of a darker red color and finely granular surface, corresponding mostly to atrophic, and at times calcified, hyalin glomeruli. Sometimes minute or larger cysts, up to the size of a pea, jut out on the surface formed by the distension of inactivated cana-aculi, (rarely of Bowman's capsules), by watery fluid or colloid masses of ilmber brown color. Some may have white calcified contents. On section the cortex is narrow; corresponding to the depressions, the visible arterial branches are stiff, thick and contorted; they project, wide open or narrowed. The change in one kidney is often more advanced than in the other.

Atrophy of the glomerulus proceeds by occlusion, collapse, hyalin swelling, or hyalin thrombosis of its capillary loops; the epithelium is lost and it becomes a homogeneous globule, poor in, or devoid of, nuclei. Perhaps it calcifies. When the capsular epithelium is also lost, the homogeneous globule becomes intimately fused with the capsule. An atrophic glomerulus is impermeable to blood and the vas afferens may connect immediately with the vas efferens. (Thoma.) According to Dehoff, there are two ways open to the blood stream when a glomerulus is totally occluded: (*a*) through branches which leave the vas afferentia before it enters the glomerulus; (*b*) the afferent vas is not the upper end of the interlobular artery, but a direct prolongation of the latter which separates into two or three twigs ramifying in the interlobular capillary network of the cortex. Atrophy of the glomerulus is followed by atrophy of its urinary tubule. (Extending a definition of Ponfick, which does not include the glomerulus, the glomerulus with its tubule may be considered a unit, called the nephron.) The high epithelium of the convoluted tubules becomes low, cuboid, or flattened; the nuclei remain, but stain intensively with nuclear stains. The tubule as a whole is narrow, but still lined with epithelium, or the epithelium lies scattered within the collapsed tubule. When the epithelium is then completely destroyed, by progressive atrophy, fatty degeneration, or other change, the uriniferous tubule collapses and is completely obliterated. The connective tissue in the atrophic area is not materially increased, but is relatively more prominent and at times may contain small groups of lymphoid cells. If numerous larger arterial branches are involved, many atrophic areas coalesce and sometimes the organ shrinks quite markedly (arteriosclerotic contracted kidney, arteriosclerotic atrophy). Aschoff speaks of "nephrocirrhosis" in all cases of contracted kidney, even in old infarcted kidneys, and in the scars of injury. Orth has voiced rational doubts in reference to the wisdom of this designation, since by the term "cirrhosis" is understood a diffuse new production of shrinking fibrous connective tissue. Neither infarctions nor traumatic cicatrices have any similarity to this. Nevertheless many have adopted this designation, *e.g.*, Lohlein, who first spoke of "nephrosclerosis," a poor name because it restricts to merely the consistency. But if this contracted kidney becomes small and rough grained, the question of combination of arteriosclerosis of numerous arterial branches with arteriolesclerosis, which is not rare, must be carefully investigated; (see Lohlein). Macroscopical diagnosis may easily err. It is important to have clinical data in such cases, and naturally an hypertrophy of the heart, if present, must also be taken into consideration.

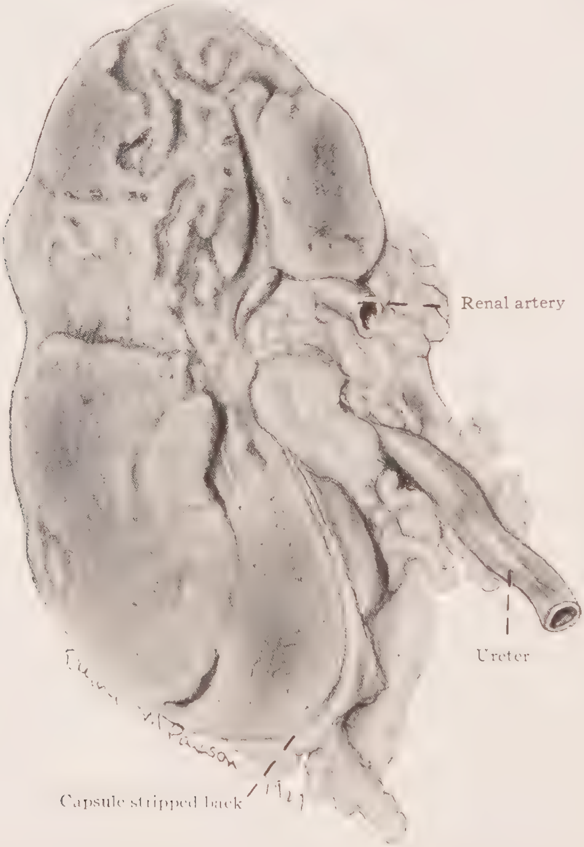


FIG. 682.—Arteriosclerotic scars in kidney of man 78 years old who died of myocardial decompensation. The ordinary chemical functional tests of these kidneys were good, the process being one of replacement, the intervening kidney structure remaining fairly well preserved. L. H.

The clinical symptoms of pure arteriosclerotic atrophy usually confine themselves to albumen in the urine; hypertony and cardiac hypertrophy are absent; according to Lichtowitz, the diagnosis is mere conjecture.

In arteriole-sclerotic atrophy of the kidney, the process is quite different; this is a primary sclerosis and atheroma of the most minute renal arterioles, especially the vasa afferentia, without arteriosclerosis of the aorta. The kidney is called true contracted kidney (arteriolesclerotic) or granular atrophic kidney. It is a disease of earlier and middle age and is accompanied by similar arteriole changes in other organs; hypertension and cardiac hypertrophy are constantly present. (See p. 1348 for the details.)

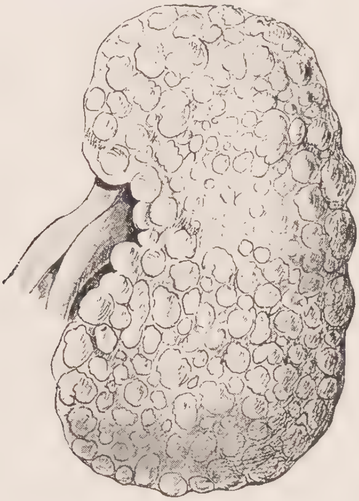


FIG. 683.—Typical arteriosclerotic atrophy of kidney in general arteriosclerosis; predominant participation by individual branches of renal artery; nat. size.

Hematogenous Degeneration and Non-suppurative Inflammation of the Kidneys

Etiology.—Hematogenous degenerations—cloudy swelling, fatty degeneration and necrosis—have this much in common with the non-purulent diffuse hematogenous renal inflammations: they result from a pathological condition of the blood which contains deleterious substances. The consequences are shown diffusely in both kidneys, very exceptionally in one only; when various poisons, metallic or bacterial, reach the kidneys by way of the blood, the glomeruli are injured or the epithelium of the tubules which eliminates some of the most important catabolic products of metabolism. Injury is done not only as the poisons are excreted, but perhaps also via the surrounding capillary blood supply, the possibility of which is clear from the circulatory conditions as described on page 1313. Reabsorption, *i.e.*, secretion by the glomeruli, and absorption by tubules is a third mode of action. Poisons may be eliminated by the cortex and reabsorbed by the loops as in vinylamin poisoning. (Oka.) There result (1), anatomic changes in the glomeruli—the so-called renal filters—

(but really more than filters, they are the most important water excreting apparatus), or functional disturbances from paralysis of the vascular apparatus, and (2) changes in (*a*) the epithelium, wherein the most important functionally and the most sensitive parts of the cortex—the convoluted tubules—are first involved with later participation by the intermediary portion and Henle's loops where the poisonous urine is concentrated. Degeneration may be slight as in diphtheria, or profound as in bichloride of mercury poisoning. This is designated by most authors as parenchymatous degeneration. Some injurious substances act more intensely on one or another part and the total damage is greater, particularly to glomeruli; there are exudation and cell proliferation of the epithelium as well as the interstitial tissue. But if the latter participates, the process must be designated as true inflammation.

Among the deleterious substances might be mentioned: (*a*) poisons introduced into the body from without to be eliminated by the kidneys either unchanged or after some alteration. Of these we may consider mercury and its salts, especially the bichloride, phenols, (carbolic acid, see Uyeno, lysol), oxalic acid, chrome salts, cantharidin, phosphorus, arsenic, sulphuric acid, iodoform, lead, (in acute poisoning), turpentine (after injections), balsam copaiba and cubebs, styrax, naphthol, pyrogallic acid, the latter even after external application. (*b*) Pathological products of metabolism may be reabsorbed and excreted by the kidneys, (autointoxication), as in gout, diabetes, icterus, hemoglobinemia, burns, chronic diseases of the skin, in pregnancy, etc. (*c*) But the toxins of bacteria comprise the largest and most important group, whether as in suppurating tumors, abscesses, etc., or in the infectious diseases, including syphilis. It is customary to think of circumscribed inflammatory foci as the result of bacteria themselves, while diffuse changes, especially degenerations of epithelium as in diphtheria, cholera, pneumonia, etc., are due chiefly to toxins, although bacteria alone may cause cell degeneration, and toxins alone may call forth extensive cellular infiltrations. (Brault and Courcoux.)

Such substances as metallic poisons or cholera-toxins produce chiefly degenerative changes with no inflammatory symptoms except secondarily; others, especially from bacteria cause not only degeneration but also exudation and proliferation, *i.e.*, true inflammation. One poison may be essentially epithelial, another glomerular. The first named changes are classed as simple toxic, or purely degenerative, or regressive, or simple parenchymatous, and are differentiated from inflammatory diseases, nephritis, and the degenerations developing secondarily in these conditions.

(In regard to the conception "Bright's disease" under which is summed up all hematogenous, bilateral non-purulent, non-specific renal affections, as well as some bilateral renal diseases due to primary vascular changes, (Fahr) and also in reference to special forms of nephritis see lit. in appendix.)

In studying acute degenerations of the kidney we meet a disease complex closely related to true nephritis, frequently designated as "nephrosis," consisting of albuminuria, edema, oliguria, cylindruria, with absence of hypertension and cardiac hypertrophy. It either leads quickly to death if the epithelial necrosis is extensive, or, more frequently, to complete recovery. The regenerative power of the epithelium is quite marked. If the degenerative changes persist for a long time, however, reactive inflammatory processes appear in the interstitial tissue, and round cells and connective tissue are deposited even to the point of the formation of scars with contraction of the organ, *e.g.*, in bichloride of mercury poisoning (Roussel). This end result is unusual.

The Differentiation of Degenerative (Regressive) from Inflammatory Changes; Various Nomenclatures

While the majority of authors agree to a separation of degenerative (regressive), from inflammatory (characterized by exudation and proliferation) renal diseases, Aschoff sees in cloudy swelling, hyalin droplet formation, and fatty degeneration, the expression of a parenchymatous inflammation, and for this reason speaks of "tubular nephritis" in all cases in which the following factors are at work: poisons mentioned under *a*, autointoxications *b*, and bacterial toxins *c*. By parenchymatous inflammation (Virchow), Aschoff pictures a defensive reaction of the tubular epithelium against an inflammatory irritant; this is possible only if the irritant (or injury) is not sufficiently powerful to kill the cells at once, for then any defense is impossible. But when the irritant is less powerful, swelling, secretion, enlargement and increase in granules take place; colloid droplets collect, fluid vacuoles and fat droplets appear, all of which represent defensive reactions—signs of inflammation—to destroy, weaken, or expel the injurious substance which has upset the biological system. This is not to lose sight of the fact that hyperirritation may finally kill the cell. Notwithstanding the interest and usefulness of this conception, (Oertel), Marchand, among others, recently has urged the theory dividing essential degenerative changes from true inflammations, and Lubarsch, considers doubtful the differential signs between parenchymatous cloudy swelling, and parenchymatous inflammation, and vigorously maintains that the designation "itis"—inflammation—should be used only if the sum total of all inflammatory reactions in cells and tissues are present, and not if only isolated reactions occur. For the present, therefore, the old conception may be retained, especially so, because clinicians consider it necessary to separate the non-inflammatory from the inflammatory diseases. Thus Fr. v. Muller proposed calling all non-inflammatory renal diseases "nephroses," in contradistinction to "nephritis" in which there should be the recognized signs of inflammation, exudation, proliferation, etc. Volhard and Fahr confine the use of this name to purely degenerative processes, and Strauss uses a still more restricted term "tubular" or "epithelial nephrosis." Nephrosis, primary degenerative disease of renal epithelium, is clinically characterized by large quantities of albumen in the urine, marked edema, cylindruria, lack of erythrocytes in the sediment, and no increase of blood pressure. Fahr includes almost all the experimental pathological processes in the kidney in this group; in fact, all renal affections in which, either directly or after cloudy swelling (1st stage), degenerative processes appear in the epithelium of the tubules (2nd stage), and are followed by reactive processes of the connective tissue and compensatory overgrowth of tubular epithelium (3rd stage). The 4th stage includes focal connective tissue proliferation combined with considerable destruction of tubules and contraction of the organ. (Consult the doubts of Lohlein and Stoerk.)

Aschoff has chosen the term "nephropathy" in place of nephrosis, and no objections can be raised if this indifferent designation is used to emphasize the non-nephritic nature of a renal disease which shows the symptoms mentioned, although in the author's opinion the term has hardly any advantage over "nephrosis." But Aschoff has given to the term "nephropathy" such a wide meaning that it becomes too indefinite since he even speaks of "nephropathia carcinomatosa" instead of renal carcinoma, and of nephropathia cystica instead of cystic kidney. Nevertheless many authors have adopted the term "nephropathy" and according to the author's opinion have needlessly sacrificed "nephrosis." Thus Lichtwitz speaks of "epithelial nephropathy" or "tubular nephropathy" as in the bichloride or cholera kidney, advising its use as a "neutral" designation in relation to the etiology. Herxheimer discards the syllable "pathy" since it implies a condition, and proposes for simple degenerative processes the designation "degeneration of the kidneys," *i.e.*, "nephrodystrophies." Altogether in reference to nomenclature there is as great a lack of uniformity as before; perhaps it has been increased by the controversy over the conception "inflammation."

The Several Forms of Degenerative (Regressive) Parenchymatous Changes. Cloudy Swelling (Albuminous or Granular Degeneration).— The epithelial protoplasm becomes cloudy, granular, the cells absorb liquids, swell, and narrow the lumen of the tubules. The striated border remains. There is frequent formation of giant cells (see Wittich). According to Dibbelt, who views cloudy swelling as a parenchymatous inflammation (Virchow), the cell structure remains intact in every detail. The cells are easily separated from the membrana propria. The nuclei may be obscured by the granules, or swell and finally disappear. The granules consist of albumen, dissolve easily (disappear) in acetic acid, and are insoluble in alcohol and ether. The convoluted tubules are the most sensitive and most highly organized and the most frequently involved. It is necessary to differentiate postmortem changes. Macroscopically, the kidney is cloudy pale gray as if boiled, with a slight broadening of the cortex.

Course.—Cloudy swelling may regress, but it is unsettled whether it ever progresses to fatty degeneration. Landsteiner thinks that cloudy swelling is an autolytic process; Orgler observed "protagon" in the form of doubly refracting granules, (see p. 1320), which were less soluble in the autolytic processes, or were precipitated during their course; Albrecht thinks otherwise, and considers it a separation or disintegration into droplets (comp. Lohlein, lit.); Aschoff believes there is merely the swelling of granules normally present.

Etiology.—It occurs in connection with the various infections such as typhoid, sepsis, scarlet fever, etc., and we will meet it again in acute nephritis.

Fatty and Fat-like Degeneration (Appearance of Protagon).—Fatty degeneration appears independently, or develops from cloudy swelling, usually between the calices, especially those subcortical, after which the glomerular epithelium degenerates, and then that of the convoluted tubules, (Ribbert, comp. also Prym), in which position the change is most marked. Microscopically, the milder degrees show heaping up of shiny fat granules and larger droplets in the bases of the cells alongside of the tunica propria. The droplets are insoluble in acetic acid or in a potassium or sodium hydroxide solution, but soluble in alcohol and ether. They stain brownish-black with osmic acid and red with sudan III. Later, the fatty granules and droplets are so numerous that the cell borders and nuclei are almost completely obscured. Many cells become detached and fall into the lumena of the tubules; others disintgrate into droplets and granules until the lumen is quite filled. But cells filled completely with fat also remain intact in situ. In marked degrees the cells appear microscopically silver gray to black. (Figs. 684 & 685.) Involvement is in foci and different areas show different degrees of severity. Sometimes only the intermediate portions are involved where it is assumed that concentration of urine takes place by absorption of water. But fatty granules are seen also in the interstitial tissue (absorption). A more irregular fatty degeneration in contradistinction to the systematic as in anemia, diabetes, phthisis, congestion, etc., was found in nephritis by

Segawa. In nephritic processes, besides the fat, there is a fat-like or lipoid doubly refracting substance which may be even more abundant than the fat.

This doubly refracting substance (anisotropic), is recognized in the polarisation microscope by its bright appearance in a darkened visual field with crossed Nicol's prisms.

These myelin or protagon droplets appear in the epithelium (myelin metamorphosis, Kaiserling and Orgler), and with disintegration of the cell are liberated or absorbed through the basement membrane into the interstitial tissue. Here they lie, phagocytosed in connective tissue cells which resemble the so-called xanthoma cells (see fig. 701); in paraffin preparations the cell contents are extracted. The clumps or heaps, in fresh unstained preparations appear as doubly refracting, colorless or pale yellow bodies. (Lohlein.) In formalin-fixed frozen sections, there are slightly arched needle-like crystals between, in, and on the clumps. (Fig. 686.) They stain with sudan III somewhat like fat, but more yellowish-red, and remain doubly refracting after quick staining. By heating and melting, the needles can be reduced to anisotropic clumps again, (sphero-crystals). As Stoerk has shown, they can also be demonstrated in formalin frozen sections stained with hemalum embedded in glycerine or in diluted formalin. The substance reacts chemically like fat, being soluble in alcohol and resistant to acids and alkalies. According to Panzer, it is a cholesterin-ester with fatty acids, at least that in the kidney, while true protagon—brain protagon—contains nitrogen and

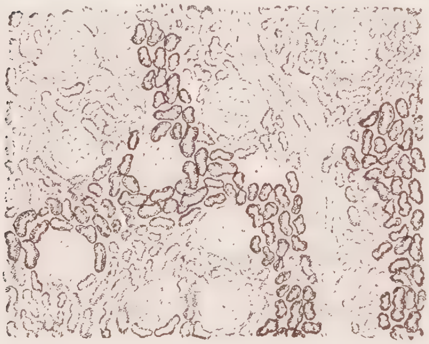


Fig. 684.

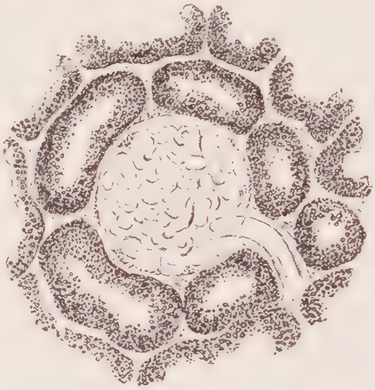


Fig. 685.

Fig. 684.—Spotted fatty degeneration, chiefly in convoluted tubules in an amyloid kidney. The amyloid glomeruli are transparent. Unstained section examined in saline sol. (Low power.)

Fig. 685.—Fatty degeneration of epithelium of convoluted tubules in an amyloid kidney. The glomerulus in center of illustr. shows amyloid degeneration and amyloid in afferent vessel, also some epithelium with fatty degeneration; fat granules in interstitial tissue; unstained section, fresh. (Medium magn.)

phosphorus. According to Orgler, its presence is due to a crystallizing-out process.

Stoerk considers it a product of protoplasmic catabolism, a view quite probably correct. (Comp. lit. of W. H. Schultze and Aschoff.) Macroscopically, the fatty degenerated areas are cloudy, yellowish, and often show small stripes and spots in the cortex while diffuse fatty degeneration gives a pale yellow color. Protagon, if contained abundantly in the epithelium and especially in the connective tissue cells of the interstitium, instead of the yellowish color, gives a dull white diffuse or spotted appearance, and sometimes the impression of an injection of the lymphatics as in fig. 686 (Lohlein). Cases have been observed in which the amount was far more than the fat. According to Munk, certain nephroses obtain a characteristic stamp by containing lipoids (lipoiduria) in the urinary sediment; lipoid nephrosis in its purest and primary form is due to syphilis. The kidney of pregnancy also belongs to this group. Lichtwitz, on the other hand, thinks the importance of the lipoids is too little understood to utilize them in the diagnosis and classification of any particular symptom complex.

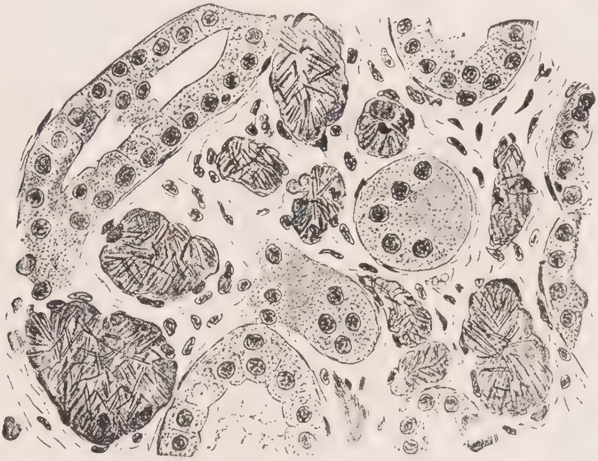


FIG. 686.—The renal interstitial tissue shows very marked accumulation of doubly refracting lipoid substance; chr. glomerulonephritis (large white kidney); woman 44 years old; about × 260.

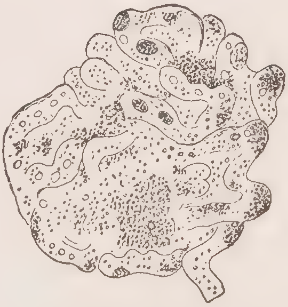


FIG. 687.—Fatty degeneration of glomerulus epithelium (after Cornil and Ranvier). (High power.)

Etiology.—Fatty degeneration depends on the substances supplied by the blood and probably also on a decrease in the oxygen supply of the cells. We see fatty degeneration in acute and chronic anemias (page

1302), in diabetes, (diffuse fatty degeneration of the cortex), in Basedow's disease, in chronic obstructive hyperemia (fatty kidney of cardiac disease, page 1301), in amyloid kidney (fig. 684). There is also a large group of chemical poisons, phosphorus among them (in the phosphorus kidney doubly refracting lipoids are absent, all the fat is isotropic fat), arsenic, sulphuric acid, nitric acid, hydrochloric acid, chloroform, iodoform, also toxins produced by bacteria and during various infections, in acute yellow atrophy of the liver, in many focal diseases, suppurating tumors, pus pockets, etc. in which fatty degeneration appears. Carbon monoxide poisoning causes decreased oxygen absorption. The fatty degeneration of phthisis results from toxemia from absorption from cavities and other ulcerations. According to Landau, the possibility that fat is being excreted in arsenic, chloroform and phosphorus poisoning, must be considered, since it collects especially in the proximal convoluted tubules, a thought further emphasized in phosphorus poisoning and acute atrophy of the liver by their lipurias. Fahr includes the kidney of diabetes in this group.

It is important to remember that normal human kidneys have fat infiltration amounting to approximately 11%, but there are no lipoids (Lohlein, Stoerk, v. Hansemann). Prym, however, believes the physiological amount is small and any quantity at all is pathological. According to W. Fischer, fat is normal in the intermediate parts, the thick limbs of Henle's loops, and frequently in the collecting tubules, but not in the convoluted tubules; in these the fat infiltration of pathological conditions is local in contradistinction to systemic fat infiltration. Fat-containing pigment is always found in the thin limbs of Henle's loop in individuals over 20 years of age. (See Segawa in reference to the kinds of fat in the kidneys under physiological and pathological conditions.) At all events, the fat is either taken up by the epithelium as neutral fat from the blood or is synthesized from soaps. The actual deposition takes place in the form of basally placed granules of different sizes in the different sections of the tubules, since the metabolic processes occur in the plasmosomes, the elementary cell substance, and vary for the individual tubules. (Arnold, Fischler.) (See Babes, Prym for more details in relation to fat in the interstitial tissue and within the renal vessels.)

But not all of the fat becomes visible with the usual fat stains; special methods are required (see Noll, comp. Pfeiffer), to dissolve the cell protoplasm and make certain lipoids microscopically demonstrable. (Diering.)

If preformed fatty substances become visible after injury to the cells we speak of fat phanerosis.

Hyalin Droplet Degeneration (see fig. 688-a).—Hyalin droplets are irregularly distributed in the protoplasm, especially of the convoluted tubules. The smallest compare with the granules of cloudy swelling but most droplets are larger and easily seen in any stained microscopic preparation. Cell borders remain intact but the cells enlarge and narrow the lumen to complete disappearance in places. Nuclei stain quite well. This change is found in all renal diseases with albuminuria; it is probably most extensive in amyloid kidney but also marked in the so-called large white kidney independently or depending possibly on glomerular changes. Landsteiner and Stoerk, (lit.), interpret hyalin droplets as "hypersecretion;" according to Fahr the droplets, also found in the walls of glomerular capillaries, have nothing in common with Altmann's granules, as Pfister assumes, but perhaps are fibrin particles; this latter idea places the change among inflammatory processes. Wegelin believes they are collections of protein bodies from which the injured cells cannot free themselves quickly enough. According to Gross, the change can be repaired. It can be accepted that extruded droplets may form hyalin casts. (See p. 1326.) It may be combined with cloudy swelling and fatty degeneration in the same cell, also with droplets of doubly refracting substances.

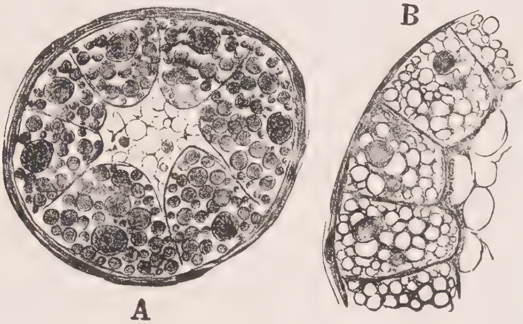


Fig. 688.—A. Hyalin droplet degeneration. B. Hydropic, vacuolar degeneration of rena epithelium in chronic glomerulo-nephritis in man 22 years old; × 500.

Hydropic, Vacuolar Degeneration (see fig. 604-b).—The epithelium swells from absorption of fluid, becomes clear and enlarges so that, as in hyalin droplet formation, the lumena of the tubules almost or quite disappear. Usually the protoplasm is foamy and contains innumerable non-staining droplets which appear like spaces in a very close, irregular, finely grained network representing the protoplasmic remains. Hyalin droplets may appear here and there in the substance of this network. (See above.) In other cases larger clear vacuoles are formed within the cell (vacuolar degeneration) which may not enlarge. (Stoerk.) This type was frequently seen by Jaffe and Sternberg in such cases of chronic dysentery in which nephritis could be diagnosed clinically. The swollen nucleus may be nothing more than a clear bubble. Finally both cytoplasm and nuclei dissolve with occasional cells visible for a longer time; basal parts of cells persist the longest. With it may be combined the formation of hyalin droplets. (See under C.)

Necrosis of Renal Epithelium.—Necrotic epithelium is distinguished chiefly by its non-staining nuclei. The protoplasm is at times cloudy and granular; at other times pale, homogeneous, or lumpy. Granules are absent in dead cells. The nuclei may disappear completely. The cells are readily detached from the basement membrane. Necrosis may occur along or combined with cloudy swelling, and fatty degeneration.

Etiology.—Pure tubular epithelial necrosis is seen most frequently in various poisonings (toxic necrosis), such as bichloride, chromic acid or hydrochloric acid salts, bile acids, cantharidin. The long continued use of sulphonal, as seen by the author in a case published by R. Stern, caused epithelial necrosis with hematoporphyrinuria. The toxins of various infections such as typhoid, (see also M. B. Schmidt), pyemia, cholera (p. 1302) may produce necrosis with or without cloudy swelling and fatty degeneration. It occurs also in diabetes (fig. 689) particularly in the convoluted tubules probably from incompletely oxidized fatty acids such as beta-oxybutric, which, as is well known, changes by oxidation into acetoacetic acid and then into carbon dioxide and acetone. In reference to the glycogenic infiltration of diabetes mellitus, see below.

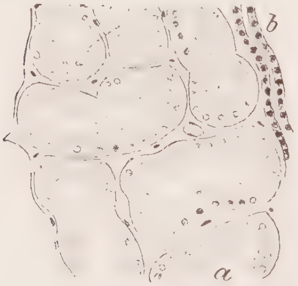


Fig. 689.

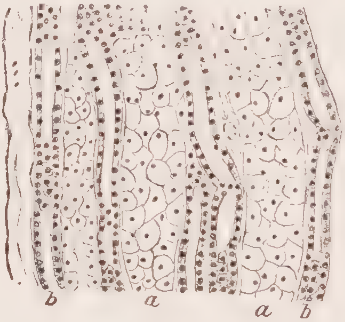


Fig. 690.

Fig. 689.—Necrosis of epithelium of convoluted tubules (a) in diabetes mellitus; b, straight tubules well preserved; 20 year old girl; 7 %–8 % sugar in urine; daily quantity 7 to 8 liters. Death from diabetic coma in spite of infusions of sod. bicarb. solutions.

Fig. 690.—Vesicular transformation of the epithelium of straight urinary tubules (a) due to glocogen infiltration in diabetes mellitus. Other straight tubules (b) are unchanged. (Medium magn.), part of medulla from same specimen as fig. 689.

Glycogen Infiltration of the Epithelium in Diabetes (fig. 690).—In the epithelium of Henle's loops, according to Baehr, more so in the "pars recta" (straight section of the convoluted tubules), sparingly in other tubule cells, in the cells of Bowman's spaces (Loeschke), and in the glomerular epithelium, glycogen appears in both granular and small and larger droplet form. As the droplets coalesce the epithelium becomes glassy. The lumena of the tubules contain granules and droplets, and glycogen-containing casts. When the glycogen is extracted with water vacuoles remain in the cells. (Fig. 690.) Even the nuclei may contain glycogen. (Huebschmann, Sussengluth.) This change, not found in every diabetic kidney, was first described by Armanni and then by Ebstein, while Ehrlich demonstrated its nature as an infiltration with glycogen. According to Arnold (lit.), the metamorphosis of glycogen occurs chiefly through the plasmosomes, *i.e.*, the granules; according to Baehr and Fahr, it is a secretion, but according to Loeschke, an excretion from the glomeruli.

Sometimes the change can be recognized macroscopically as a brown discoloration after pouring Lugol's solution over the kidney, but Best's carmine stain gives the best results. (Comp. p. 950.)

Glycogenic infiltration may be present with epithelial necrosis, (fig. 689), but Fahr thinks this is a post mortem autolytic process; it is more frequently associated with diffuse fatty degeneration, but without "protagon," (comp. Stoerk). According to Klemperer, it is pure fat infiltration; according to Fahr, fat storage caused by lipemia. Ether extracts of diabetic kidneys may yield over 22% fat, while normally at its highest, it is 11%.

See Frank in reference to so-called renal diabetes in which the kidneys are unable to retain the glycogen normally present in their protoplasm.

Albuminuria. Urinary Casts

Albuminuria.—Albuminuria or the appearance of albumen in the urine is clinically the chief symptom of injury to the secretory parts of the kidney—the renal cells and membranes. The source of the albumen is essentially the blood; it consists of both serum albumen and serum globulin, the former usually in much larger quantity. Traces of albumen are occasionally found in every urine, and even a somewhat more marked albuminuria (up to 5%) may still be physiologic, *i.e.*, be possible with normal kidney function (Leube). The so-called physiologic albuminuria passes into the pathologic without sharp boundaries.

Constitutional, juvenile, or orthostatic albuminuria is probably caused by disturbances of the nervous apparatus of the kidney, and is frequently classed with physiologic albuminuria. The patients not unusually show degenerative tendencies, the albumen is passed while in the standing position, and lordosis of the lumbar spinal column may be a causative factor. No albumen is voided while the individual lies down. It is not a disease, but a peculiarity, or a symptom. (Caranfilian, Lichtwitz.)

Pathological albuminuria is probably always due to renal changes consisting of circulatory disturbances alone, or disease of the renal tissue itself, even though an anatomical change is not always demonstrable, perhaps from lack of freshly fixed material. It is a remarkable fact that the most marked albuminuria is not by any means always in glomerulonephritis (glomerulitis), but in disease of the tubular apparatus, *i.e.*, simple toxic degeneration, which is very suggestive of the proposition that the tubules are more permeable to albumen (comp. Lichtwitz).

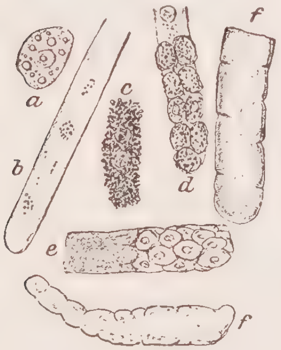


FIG. 691.—a, fat-loaded epithelial cell; b–f, urinary casts; b, hyalin; c, coarse granular; d, hyalin cast covered with fat infiltrated epithelial cells; e, epithelial cast partly finely granular; f, waxy cast.

Urinary Casts.—Urinary casts are casts of the tubules, most frequently of Henle's loops. They are always a sign of renal disease, however slight, and according to their structure, permit deductions at times as to the type of pathologic anatomic changes present in the kidneys. They are "messengers of renal processes" (Frerichs). Three groups may be differentiated: (1) Those formed of cells only: (*a*) epithelial casts from detached actual epithelial tubes, or compressed single cells, well preserved or degenerated in various ways (fatty, granular, etc.), in which case the casts are granular; (*b*) blood casts formed by the compression of blood which reached the urinary tubules; the corpuscles are more or less changed in form and color and are held together by fibrin coagula. Blood pigment casts are granular, brown to reddish-brown cylinders consisting of blood pigment alone, or of granular blood pigment on hyalin casts. Casts of leucocytes are very rare, but a layer of leucocytes on other casts is found quite frequently. (2) Coarse and fine granular casts consist of minute fat granules, staining black with osmic acid and red with sudan III, or of granular masses of albumen; they are derived from disintegrated epithelium, perhaps also from disintegration of previously homogeneous casts. (3) Amorphous, structureless casts: hyalin casts are the most frequent of urinary casts; they are pale, transparent, sometimes very long, kinked, stretched, soft and pliable. They stain with iodine or carmine and are then easily seen. They are soluble in acetic acid and in hot water, and disappear quickly in alkaline urine. Not infrequently all kinds of substances are superimposed such as red and white blood corpuscles, renal epithelium, albumen or fat granules, leucocytes filled with fat droplets of degenerated cells, urates (uric acid salts), calcium oxalate, hematoidin granules derived from disintegrated blood, bacteria; the casts may even serve the latter as culture media. They appear not only in the various forms of renal disease, but also in the most varied, often unimportant renal irritations such as the so-called physiological albuminuria mentioned on page 1325, in icterus, heart lesions, chronic constipation without albumen (W. Ebstein), the albuminuria of the newborn, and other forms of albuminuria in which inflammatory renal changes cannot be demonstrated anatomically.

Formation.—There is a variety of opinions as to the formation of these casts. They consist of albumen, from two main sources: (*a*) albumen of the blood serum, (*b*) epithelium of uriniferous tubules; some add to this, fibrin. It is considered that transudation of serum albumen is frequent through the glomeruli; this is changed, from fluid, to solid form in the tubules. The coagulation may be initiated by dying leucocytes and epithelium. More recent conceptions regarding the formation of casts from coagulation assume that it is due to colloid chemical processes. (Lichtwitz, Hoper, lit.) It is quite remarkable that no relation has been found between the amount of albumen and the number of casts in the urine. There may be but few casts and much albumen and vice versa. Indeed there are cases of true nephritis with a complete symptom complex and urinary casts, but no albuminuria. But soluble proteins may appear during the decomposition of cells, epithelial as well as blood corpuscles, and these may become active in cast formation. According to Senator and others, hyalin casts may also form from dying epithelium fusing into hyalin cylindrical masses, but Lichtwitz considers this unproved. According to Landsteiner (lit.), casts may form by confluence of hyalin globules which pass from intact cells into the lumen, and the author sees many preparations which can be interpreted in this way (comp. p. 1323).

Waxy casts are yellowish, dull, shiny like wax, firmer and broader than hyalin casts, with sharp outlines. There are frequent cross fractures or cracks. They develop perhaps from a colloid change in epithelial casts and therefore are called metamorphosed casts; according to others, they are older, concentrated urinary casts which remained for some time in the tubules, parts of which are never washed out. They are always accepted as a sign of severe renal disease.

Cylindroids are long, tapering pale casts of uneven width often fringed at the ends. Thomas and others think they are closely related to hyalin casts; others consider them mostly mucous threads, (mucous casts). Their source may be the kidneys or the secretion of the prostate, or of Cowper's, or Littre's glands, etc.

Generalizations in Reference to Pathologic Anatomic Changes in the Different Forms of Non-purulent Acute and Chronic Inflammatory and Non-inflammatory Renal Affections.—The changes under consideration occur in (1) the epithelium of the urinary tubules, (2) the glomeruli, (3) vessels and interstitial tissue, (4) contents of urinary tubules; the latter question has been disposed of in discussing urinary casts.

I. Changes in the epithelium of the urinary tubules (degenerative and regenerative) involve especially the secretory parts—the convoluted tubules—and the thick ascending limbs of the loops. But the intermediate parts are not spared (p. 1297). In acute inflammation, cloudy swelling is the predominant change, (p. 1318); in the subacute stage there are chiefly fatty or fat-like degenerations, (p. 1319), the formation of hyalin droplets (p. 1323), hydropic changes with formation of vacuoles (p. 1323), and also necrosis at times (p. 1324). Sometimes there is marked exfoliation (catarrhal or desquamating nephritis), which may be balanced by regeneration, the latter occurring in both acute and chronic noninflammatory or inflammatory renal diseases. But apart from these circumstances in which the regenerative processes are frequent and abundant and recognizable by karyokinesis (Thorel, Heineke, Herzog, Oertel, Wittich, the two latter emphasize the presence of epithelial giant cells, see also Lohlein, Oliver), regeneration is frequently met in infarction, abscesses, tuberculosis, traumata, experimental injuries, etc. Tilp (lit.) believes the only true regeneration is an epithelial new growth within the tubules, while the formation of entirely new tubules in focal diseases is a frustrated attempt at regeneration; they may secrete, but are insufficient in a morphological and functional sense. Desquamated epithelium (and casts) may choke the tubules and cause urinary stasis (Ponfick), but some deny that this can cause atrophy of the glomeruli involved. (Comp. p. 1311, see Jores and comp. opposite view Loehlein.)

All kinds of degeneration and atrophy in the tubular epithelium occur in chronic renal diseases; there may be complete disappearance of whole tubule groups, especially the convoluted tubules. Destruction may be due to primary epithelial changes, or secondary to the death of glomeruli which determines to an essential degree the fate of the parenchyma. Healthy parts may undergo compensatory hypertrophy. Enderson's investigations of the compensatory hypertrophied human kidney and those of C. Hirsch on animals, show that cells with increased function have an increase in granules. (Comp. Casa-Bianchi.) It would be interesting to know whether the same phenomenon is present in the hypertrophic epithelium in chronic renal diseases; quite fresh material is required for investigation.

II. Glomerular Changes.— We understand by the term glomerulus or Malpighian corpuscle not only the actual capillary loop, but also Bowman's capsule covering it. Many glomerular changes are so slight that we can derive conclusions as to a change in the capillary loop only by: (*a*) demonstration of albumen within the capsular space, by fixation in absolute alcohol or formalin, or by the boiling method of Posner. (P. 375.) The albumen coagulates in granular, or less often in hyalin form. (Fig. 692.) Sometimes hemoglobin is also made visible by these methods as a yellow brownish color. Blood enters the capsular space by diapedesis, in hemorrhagic renal inflammations (hemorrhagic glomerulitis), and leucocytes also escape from the capillary loops. Occasionally true stringy fibrin can be demonstrated within the capsule with Weigert's stain. Adhesions may result from secondary connective tissue production (adhesive glomerulitis, Engel, see also Harvey). (*b*) Changes in the cells of the capillary loops and of Bowman's capsule can be recognized in acute inflammations as granular and cloudy swelling, fatty degeneration, necrosis and desquamation; some loops are completely denuded of their epithelium. The desquamated degenerated epithelium then lies within the capsular space and mingles with red and white blood corpuscles and fibrinous and hyalin masses. The condition may be called desquamative or catarrhal glomerulitis. On the other hand, some glomeruli with their capillary and capsular epithelium are perhaps in active proliferation so that multiple concentric layers (crescents) are developed which are attached more closely to the capsule (this often shows splitting) than to the loops and gradually fill the entire capsular space. But the epithelium of the loops and the cells between them may also be thickened and a flat

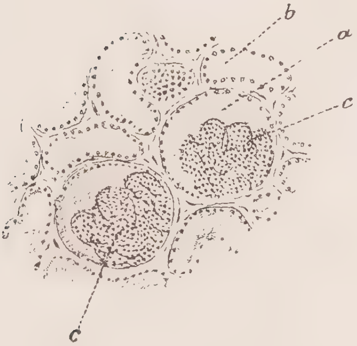


FIG. 692.

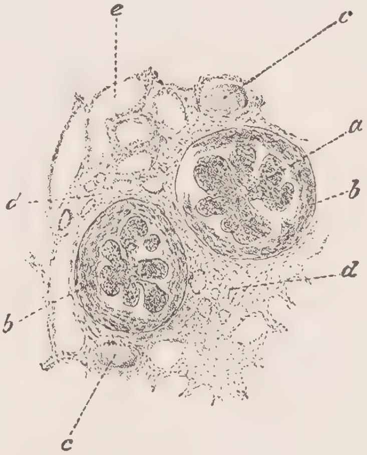


FIG. 693.

FIG. 692.—Acute nephritis in true pharyngeal diphtheria; child 4 years old; a, albumen in capsular space; b, convoluted tubule containing albumen; c, vascular loop with epithelial proliferation. Hardened in absolute alcohol. Carmine and picric acid.

FIG. 693.—Glomeruli (a) with marked proliferation and concentric arrangement of capsular epithelium (b); the loops are plump and abundant nuclei show the same changes as described below under c. Glomerulo-nephritis of 3 months standing due to scarlet fever. c, hyalin casts; d, atrophic tubules in increased interstitial tissue; e, empty meshes of dilated convoluted tubules; epithelium was lost in preparing section. (Medium magn.)

coating (Ribbert) will cover the capillaries. (*c*) The capillary loops increase in size by enlargement and multiplication of the endothelial nuclei (counts by Mertz); the lumena are thereby narrowed and filled with desquamated degenerated cells (Langhans), to which are added collections of leucocytes and thready masses of fibrin which may form hyalin thrombi. The loops then appear extraordinarily rich in nuclei (fig. 696) and their lumena are blocked. Both increase in size and mitoses are observed in the nuclei between the capillaries (adventitial); thus demarcation of the several loops is obscured and finally rendered completely gone by hyalin degeneration (swelling) of the capillary walls, narrowing and closure of the lumen. It must be emphasized, however, that these changes are recognized with difficulty, and their pathologic importance is difficult to determine. (Details by Lohlein, Herxheimer, Gross.) In the arteriosclerotic contracted kidney, Lohlein describes changes in the glomerular loops such as hardening, collection of hyalin masses within the lumen, later lipoid infiltration, increase of endothelial cells with subsequent homogenization, which he considers essentially similar to those changes found in the arterioles. Enlarged glomeruli can be seen with the naked eye as gray transparent granules.

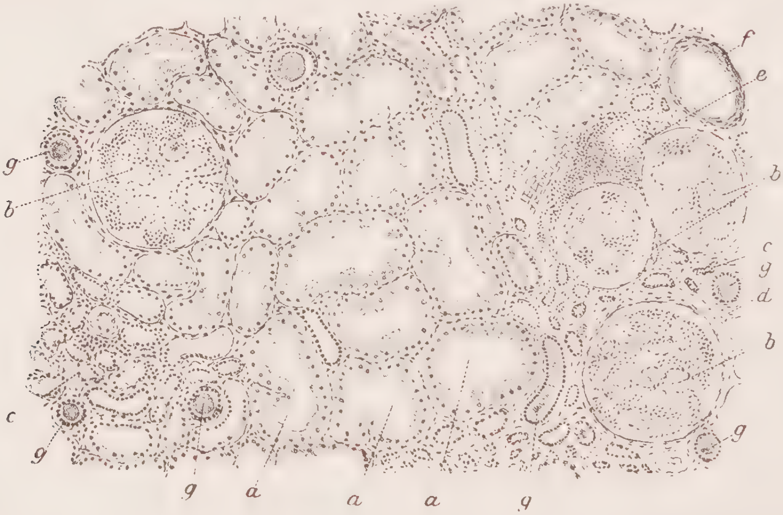


FIG. 694.—Chronic glomerulo-nephritis; large white kidney with smooth surface. a, hypertrophic, wide convoluted tubules with high epithelium; b, some glomeruli large with hyalin loops, others poor in cells and shrunken; c, atrophic tubules; d, sclerotic hyalin interstit. tissue; e, small cell infiltration; f, vein; g, cast in tubule (intermediary port.). (Medium magn.)

If the process becomes chronic, the glomeruli progressively undergo atrophy, the cellular elements disappear, and the capillary loops are occluded and fused into a homogeneous hyalin contracting globule. (Stains yellow with van Gieson stain.) The capsular epithelium may not only be preserved at the beginning but may even proliferate, but it finally desquamates or perishes from fatty degeneration. Secondary glomerular atrophy is due to connective tissue proliferation around the entrance of its vessel, or direct growth into the capsular space (Bohm, comp. Harvey). Proliferation of Bowman's capsule also compresses the skein from concentrically deposited layers of contracting connective tissue (red with van Gieson stain). Finally the atrophic glomerulus becomes a solid globular hyalin structure with few or no nuclei and fused with the capsule. (Fig. 695.) The globule may calcify. According to Baum, dots on the renal surface are not always calcified glomeruli, but may be calcium-containing cysts of the uriniferous tubules or imperfectly developed glomeruli. According to Herxheimer, hyalin glomeruli (stain bright red with van Gieson's stain) occur quite often in the newborn and are small developmental lesions. Finally, some glomeruli show compensatory hypertrophy and have wide loops.

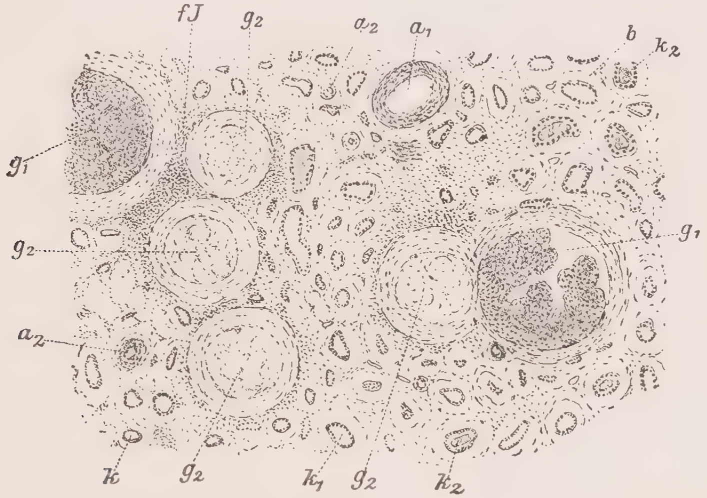


FIG. 695.—True arteriosclerotic contracted kidney. The kidney was quite small, red, nodular, firm, as in fig. 703. a-1, larger thickened hypertrophic artery; a-2, smaller thickened and narrowed arteries (arterioles); b, connective tissue broadened; f, J, fresh infiltration focus; g-1, glomeruli with hypertrophic loops and thickened capsule; g-2, obliterated glomeruli, the hyalin loops fused with the thickened capsule; k-1, atrophic tubules: k-2. atrophic tubules with casts. (Med. magn.)

(In reference to the relation of glomerular destruction to capillary atrophy see pp. 1311 and 1328.)

Changes in the Interstitial Tissues.—In acute glomerulo-nephritis the changes in the interstitial tissue are slight, such as periglomerular infiltrations of leucocytes and edema. In subacute glomerulo-nephritis round cell infiltrations (lymphocytes and plasma cells) are quite common in groups, or in severe cases, diffusely spread. These cellular infiltrations also localize in the vicinity of the cortical veins and are most marked in acute interstitial nephritis (see page 1338). If the infiltration is focal the condition may be called "interstitial focal nephritis," but the condition is only a difference of degree from the hematogenous suppurative focal nephritis due to the presence of easily demonstrated pyogenic organisms. When leucocytes are abundant, as in the focal nephritis of septic infections, bacteria are also frequently present. In very severe grades of inflammation, the interstitial tissue of both cortex and medulla is saturated with exudate, the septa are markedly enlarged and the whole kidney is swollen and soft (exudative nephritis). The fluid seen after careful fixation of the preparation, is rich in albumen; it sometimes contains fibrin and occasional erythrocytes and round cells, (inflammatory edema). The more marked the inflammatory process in the interstitial tissue, the more marked is the "firm soft" swelling of the entire organ which becomes pale and glassy, and thus can be distinguished from simple degenerative changes. In older acute nephritis with much fatty degeneration of the epithelium, fat granules are found in the interstitial tissue. (Degeneration or absorption?) In reference to doubly refractive substances see p. 1320. Hemorrhages into the interstitial tissue are sometimes found in focal form; it is only in quite severe nephritis, especially the acute interstitial form following scarlet fever, that there is a more diffuse extension.

Changes in the connective tissue play an important rôle in all chronic renal diseases. Undoubtedly proliferation and exuberance are often secondary to epithelial atrophy which in turn is often dependant, at least in part, on glomerular atrophy. The conditions are seen most clearly in the true contracted kidney in which the connective tissue is proliferating and swollen and sclerotic, but the relation between epithelial degeneration and chronic inflammatory changes in the connective tissue is difficult to determine. Indeed certain authors believe the connective tissue changes are reparative. Usually the proliferative processes in the connective tissue are considered primary and we speak of chronic interstitial nephritis, but according to Weigert's investigations it now appears doubtful if there really is a primary chronic interstitial nephritis with the epithelium involved in a later secondary injury. At present, the so-called "true contracted" kidney is considered arteriosclerotic and the connective tissue proliferation reactive or even reparative, (comp. p. 1353), although even on this point there is no uniformity of opinion. (Comp. Stoerk.)

The Different Forms of Non-suppurative Renal Inflammation

Acute Nephritis.—If we rule out the acute renal lesions classed by others as nephritis and by us as degenerations, *i.e.*, sublimate kidney, cholera kidney, etc., (see p. 1032), there are three forms of acute nephritis:

(1) acute glomerulo-nephritis, (2) embolic, non-suppurative focal nephritis, and (3) acute interstitial nephritis.

(1) The most important and by far the most frequent form is acute glomerulo-nephritis. This designation means that the process begins in the glomerulus as do most renal diseases. Without exception both kidneys are diffusely involved. The microscopic findings vary considerably and sometimes do not correspond at all with the severity of the clinical symptoms. Thus we see cases ending in death in an astonishing short time, (1–2 days of illness), either from uremia or reflexly through the central nervous system. (See Dietrich.) There may be no observable macroscopic lesions in the kidneys, and microscopically, the picture of acute glomerulo-nephritis, especially glomerulitis, is all that is found. In other cases macroscopically severely changed kidneys may be present (see below).

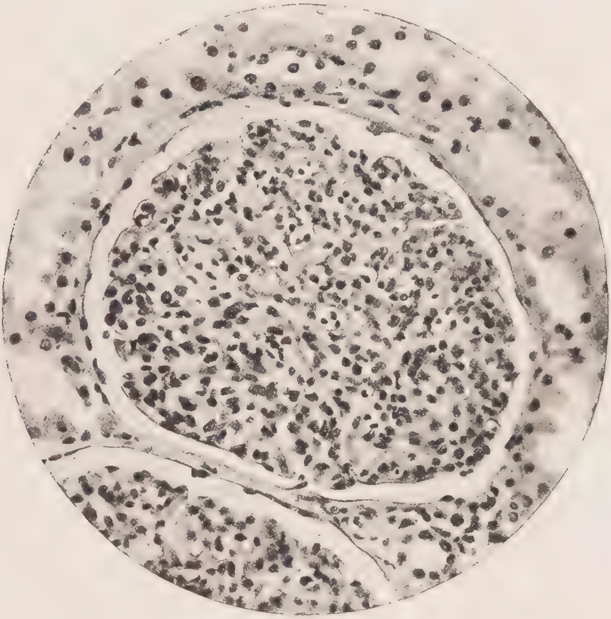


FIG. 696.—Glomerulus with abundant nuclei in acute diffuse glomerulo-nephritis. Death on 18th day of illness. (High power.) (Fahr, V. A. 225, 1918, p. 29.)

Etiologically, we blame scarlet fever, angina, tonsillitis, measles, mumps, typhoid fever, influenza, malaria, gonococcus and meningococcus infections (Huebschmann and others), but above all, streptococcus infections, (Lohlein). The form so frequently observed in the war (war nephritis) is an acute and subacute glomerulo-nephritis accompanied by marked edema, decrease of urine output, albuminuria and hematuria, but in most cases running a favorable course. Herxheimer (lit.) holds etiologically responsible the toxins of (strepto-) cocci which probably enter the body through the air passages, but the predisposing factors such as wet and cold, which have always been considered important in the etiology of nephritis, must not be underestimated. (See also C. Hirsch, Gross, lit. by Herxheimer.) Thus far it has been possible to produce experimental glomerulo-nephritis with focal dissemination only by the use of uranium nitrate which attacks the capillary endothelium particularly and produces relatively slight tubular injury. Kuczinsky produced glomerulo-nephritis in mice with streptococci.

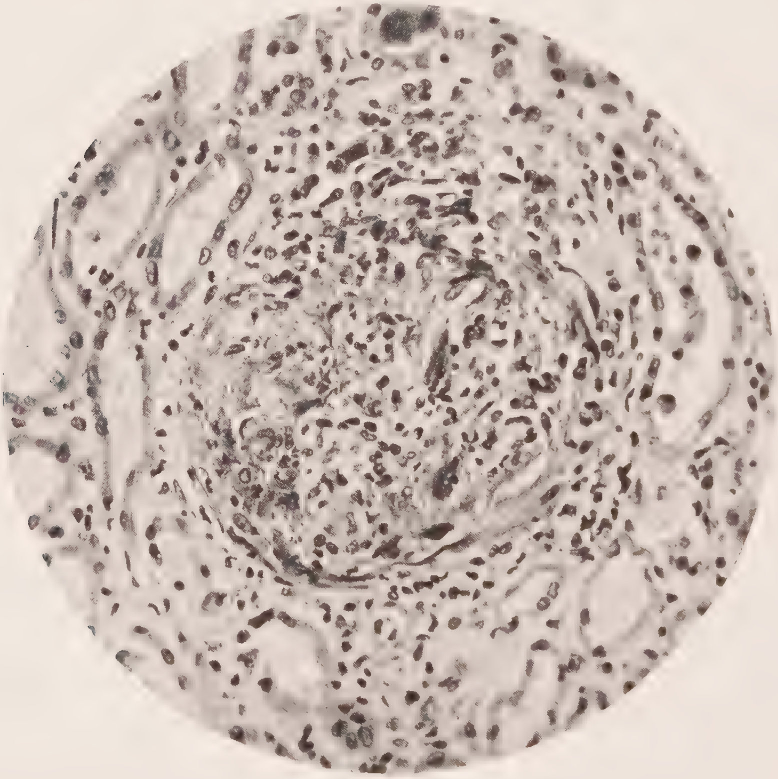


FIG. 697.—Acute capillary glomerulitis. This patient 24 years old acquired nephritis from angina. There are necrosis of the cells of the capillary loops and infiltration by inflammatory cells. This is present in practically every glomerulus examined in a number of sections so the process was not focal but diffuse. × 230. L. H. #203.

The glomerular changes as described by Langhans, Lohlein, Fahr, Herxheimer and others were discussed on page 1328. They consist of broadening and lengthening of the capillaries which contain little or no blood but numerous cells enmeshed in a network of finely coagulated exudate. The cells are in part endothelial showing cloudy swelling, proliferation and necrosis, and in part leucocytes which are also found in the capsular space and in the uriniferous tubules, and which, as Graff demonstrated, give the oxydase reaction to a marked degree. (P. 196.) In contradistinction to these intracapillary changes which cause the characteristic wealth of nuclei in the enlarged capillary skeins, the changes in the epithelium of the loops are often only slight, although consistently present; but they may progress through cloudy swelling and fatty degeneration to desquamation and proliferation. In the acute stage of glomerulonephritis, the changes in the parenchyma are, as a rule, slight, and consist of cloudy swelling to hyalin droplet formation and fatty degeneration of the epithelium in groups of tubules. The characteristic epithelial "crescents" generally appear later in the course of the disease. It must be especially emphasized that practically all of the glomeruli, indeed Lohlein states that "all of them," are usually more or less changed. Since the finer details are difficult to recognize, this description serves only in a general way and the details must be fitted to the particular case (lit. by Lohlein).

Results.—If acute glomerulo-nephritis does not heal, it becomes subacute or chronic and then, among other lesions, parenchymatous changes become extensive. (See p. 1341.)

Addition of Degenerative Parenchymatous Changes (Tubules) and Inflammatory Processes of the Interstitial Tissue to Glomerulitis.—Although pure glomerulitis does occur, a number of cases show more marked degenerative changes at once, especially cloudy swelling and fatty and hyalin droplet degeneration of the tubules, which are brought about secondarily from (*a*) glomerular injury or (*b*) by the action of the causative toxins from the lumena after passage through the glomeruli, or (*c*) through the blood of the capillaries surrounding the tubules. Macroscopically, the kidney is heavier (up to 200 gms.), considerably enlarged, soft, fragile and the capsule strips easily being under tension in vivo. Corresponding to the type of the predominant parenchymatous degeneration, the broad cortex is cloudy and grayish red, or if older and fatty degeneration has progressed further, grayish white, or yellowish white, spotted and bulging. The medulla is usually dark red and sharply demarcated from the cortex. Pronounced markings in the cortex correspond to the fatty degenerated tubules of the labyrinth in their cloudy yellowish white convolutions, and between them the grayish white glassy medullary rays. Sometimes leucocytic infiltration is early and surrounds the Malpighian bodies, (so-called periglomerulitis), and the intermediate areas; interstitial inflammatory changes appear around the veins, especially in the subcapsular cortical region. Cellular infiltration may also appear at the base of the pyramids. These cells migrate from the capillaries together with serum, and even fibrin, so that the surrounding interstitial tissue is saturated with "edema."

The kidney is thicker, moist and glassy, soft and pale grayish white because of capillary compression. On section the cortex bulges markedly, and is streaked with cloudy yellowish white stripes and spots corresponding to the degenerated tubules.

If hemorrhage is added, acute hemorrhagic glomerulo-nephritis is the result, in which numerous minute dots are seen on the surface representative of blood-filled capsular spaces. Somewhat larger angular spots correspond to groups of blood-filled uriniferous tubules belonging to one system and surrounding their respective glomeruli.

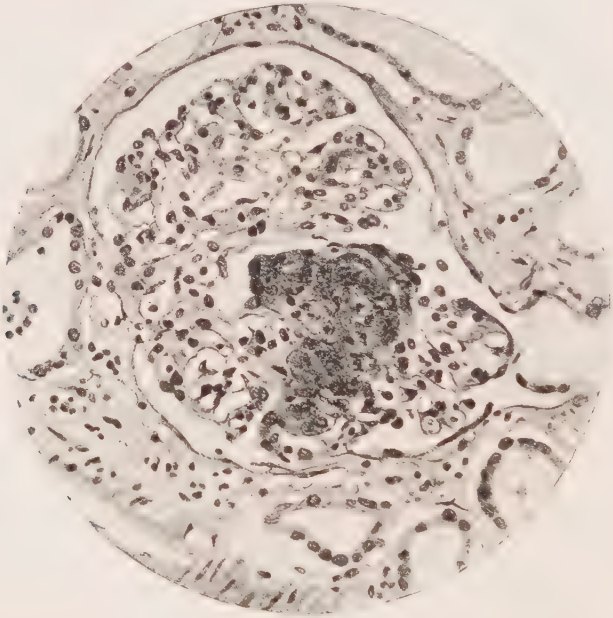


Fig. 698.—Glomerulus from embolic focal nephritis. Necrosis and homogenization of portion of loops. Fusion of altered loops with capsule. Woman 29 years old; endocarditis for ½ year. (High power.) (Fahr, V. A. 225, 1918, p. 33.)

II. Embolic non-suppurative focal nephritis (Lohlein) occupies a special place among the hemorrhagic nephritides. It is caused by multiple embolism of glomerular capillaries, especially in chronic ulcerative endocarditis, and is most often due to the streptococcus viridans s. mitior (see pp. 35 and 36) which causes endocarditis lenta, usually aortic—see Gessler.

Fibrinous plugs obstruct the glomerular capillaries, and swelling and necrosis (infarction) of one or more loops follow, with necrosis and exfoliation of the epithelium covering the loops. The loops coalesce to a homogeneous fibrinoid mass usually penetrated by fine clefts. They then fuse with the capsule, usually in several places, after which a poorly cellular scar obliterates the boundaries of glomerulus, capsule and adjacent tissue. The epithelial cells of glomerulus and capsule which escape destruction may show reactive proliferation and true crescents and confuse the picture with that of true glomerulo-nephritis. The difference consists in the wealth of nuclei in the skein. The presence of organisms in the glomeruli can hardly be proved, but in contra-distinction to typical glomerulo-nephritis, the changes are found only in single glomeruli. Rupture of capillaries leads to hemorrhage into the capsular spaces and tubules and causes the innumerable red spots on the surface; in fact hematuria is the most striking clinical symptom in these cases while nephrogenous edema and advanced qualitative urinary changes are absent; uremia is quite rare. The glomerular atrophy is followed by degeneration of the tubular epithelium but frequently to only slight degree. In the vicinity of diseased glomeruli are infiltrations of leucocytes and edema which contribute to the swelling of the kidney. Lohlein, discussing the close relationship to suppurative focal nephritis, emphasizes the relative paucity of the leucocytic reaction in hemorrhagic embolic focal nephritis. Still there are cases in which the infiltration is quite marked. Casts and leucocytes are also found in the uriniferous tubules.

Acute cases are macroscopically recognized by large discolored kidneys, and enlargement and firmness of the spleen. Progressive change to a contracted kidney in which relapses and exacerbations have occurred is rare; usually the original disease is fatal before this takes place.

The author examined a case in which only one kidney showed a chronic non-suppurative focal nephritis established selectively in the peripheral cortical areas and combined with smooth atrophy. It had been extirpated on account of prolonged profuse hematuria. The other kidney showed only a few isolated, old, reactionless striae-like atrophic areas in the cortex with atrophic glomeruli and tubules. The interstitial tissue was increased and poor in cells.

Fahr advises a sub-classification of embolic non-suppurative focal nephritis under the term focal glomerulo-nephritis in contradistinction to the diffuse; in general he classifies glomerular inflammatory changes into:

I. Diffuse glomerulo-nephritis
II. Focal glomerulo-nephritis
    1. of toxic origin (uranium poisoning)
    2. of bacterial origin
        a. non-suppurative excretory nephritis, at times more proliferative, at other times more exudative (thrombosing glomerulo-nephritis).
        b. embolic, non-suppurative focal nephritis (Lohlein). Among others, Lohlein and Herxheimer emphatically oppose the conception of focal glomerulo-nephritis.

III. In acute interstitial nephritis following angina, scarlet fever, diphtheria, etc., the enlarged, thick, soft kidneys show washed-out reddish spots alternating with grayish red or light gray areas after the capsule is stripped from their smooth surfaces. On cross section, the broad cortex bulges, is pale grayish red, cloudy, marked by red to brownish hyperemic hemorrhagic striae and spots sometimes cone-shaped, while the normal markings (medullary rays and labyrinth) are more or less obliterated; the medulla is dark grayish red and but slightly swollen.

Scattered in the cortex are microscopic foci of round cells chiefly lymphocytes which come from small vessels outside of the glomeruli. Plasma cells are also plentiful, as pointed out by Councilman, (see Landsteiner, who speaks of nodular infiltrations). Leucocytes are sparse, but occasionally numerous. These foci of pointed, striped or possibly wedge-shaped form lie more or less closely approximated within the cortex close to the base of the pyramids, or subcapsular, or between the tubules. When they surround the glomeruli they blend into large complexes and obliterate the cortical architecture. Within these foci and elsewhere there are marked epithelial degeneration and more or less abundant leucocytic migration around and within the urinary tubules, many of which are destroyed. The parenchyma distant from the foci, apart from the hemorrhages into the tubules, is usually not very markedly changed by cloudy swelling or fatty degeneration. Hyperemia and diapedesis of erythrocytes are seen at the edges of the foci, particularly in the cortex. The glomeruli are not primarily changed, although as Lohlein remarks, all glomeruli cannot be expected to be perfect. What changes are present consist of thrombosis of one or the other capillary loops interpreted as the consequence of the passage of toxins or the lodgement of infected emboli. The emboli by culture are sterile or contain only a few organisms (Councilman), and yet they are responsible for the rupture of capillaries and consequent hemorrhages. Munk saw this interstitial nephritis in hemorrhagic small-pox.

In scarlet fever nephritis, we must differentiate (Reichel, lit.) two quite different forms: (1) the interstitial multiple focal disease just described above need not produce severe symptoms because of its focal character, but if the parenchyma is more severely involved it may cause death from uremia. (2) In typical post-scarlatinal glomerulo-nephritis, Reichel believes the changes begin in the loops with thickening of the walls, abundance of epithelial nuclei, poor blood supply, filling with leukocytes accompanied by injury to the epithelium of the skein (desquamation). Exudative processes in the capsular space soon follow, (leucocytes and fibrin). Epithelial proliferation is added later (crescents) and with the growth of invading fibroblasts, adhesions and atrophy of the glomerulus follow, as described by Goemans and Engel and others (p. 1328). In some cases it leads to diffuse disease of the rest of the kidney. Soerensen recognizes a glomerulo-nephritis alone as the type in scarlet fever manifesting itself in the third week of the disease. Jochmann with Baginsky thinks that the process is essentially uniform, sometimes more parenchymatous, sometimes more interstitial, and that we cannot speak of a predominant glomerulo-nephritis, but the author supports Reichel's opinion, and shares this conception with Lohlein.

The etiology of acute nephritis has been discussed among the three forms described above.

The following is a short resumè of our conception of the action of bacteria and their toxins: if an acute nephritis develops as a complication of an infectious disease or of any infectious focus, among others, tonsillar angina, the action of bacteria and their toxins is as follows: (*a*) bacteria pass from the blood through the glomeruli, cause nephritis and then disappear in the urine; (*b*) toxic metabolic products (toxins) formed in any part of the body may be excreted through the kidneys and produce nephritis without bacteria reaching the kidneys at all; (*c*) bacteria and toxins both enter the kidneys. It need not be emphasized that the virulence of bacteria is a variable factor, and correspondingly the processes may be severe or slight, acute or slowly progressive; highly virulent streptococci may cause focal suppuration and abscess formation, less virulent bacteria may cause slow destruction of the glomerular capillaries in which they sojourn without being especially pyogenic. (See p. 1336.) On page 1316 it was emphasized that the tendency on the whole is to consider degenerative changes, *i.e.*, those which are not directly due to changes in the glomerulus belonging to the tubule, as due to toxins, while focal inflammations are thought due to bacteria. Sometimes the specific organism, that of pneumonia, of typhoid fever (rarely), of recurrent fever, even of erysipelas, has been found in the kidney as the cause of a nephritis developing as a complication of the original disease. The bacteria are present in the loops of the glomeruli, interlobular vessel twigs, capillaries of the cortex, and free in the interstitial tissue, but often also in the tubules glued to casts. As a rule no bacteria can be demonstrated in the ordinary forms of scarlatinal nephritis unless there is a special mixed infection (see pp. 612–613), when streptococci may be found, but they are occasionally found in articular rheumatism, small pox, etc. as well. In influenza, Kuczinski holds responsible the mixed infections so frequently active in the lungs. (See also Knack.) In pyemia and septicemia it is easy to demonstrate large numbers of bacteria in the kidneys especially in the glomeruli, and in the urine. These conceptions are discussed under "puerperal wound infections."

Important Clinical Symptoms of Acute Nephritis.—The urine practically always contains albumen (albuminuria); its quantity is diminished (oliguria), sometimes secretion ceases altogether (anuria). The quantity of albumen varies; it is greater in the forms with severe tubular involvement, such as diffuse glomerulo-nephritis; in acute focal nephritis the more serious functional disturbances are less evident, corresponding to involvement of fewer glomeruli and tubules; the minor qualitative changes in the urine including hematuria are explained by the changes in a comparatively small number of glomeruli. The specific gravity is usually increased, the color as a rule is dark, sometimes cloudy or bloody; hematuria, the sign of capillary lesions, is almost constant especially microscopically. On standing a heavy sediment contains uric acid, salts, and such morphologic elements as red and white blood cells, renal epithelium and especially casts. (See p. 1326.) The latter may be hyalin, granular, purely epithelial and at times blood. Sometimes casts appear before albumen. Among other symptoms may be mentioned edema, hydrops of the skin and serous membranes in varying degrees; it is especially marked in the typical nephritis of scarlet fever and with the kidney of pregnancy. Hypertony varies but, except in very light cases, is easily recognized.

Schlayer and Takayasu speak of vascular nephritis as in scarlet fever, in which injury is found, chiefly to the glomeruli with edema and disturbance of excretion,—and of tubular nephritis as in diphtheria, in which the tubules are principally affected and edema is almost completely absent. Vascular nephritis is caused by poisoning with arsenic and cantharidin, while poisoning by sublimate, aloin or uranium causes a tubular nephritis. (See Hirsch, Fahr, lit.) But again we encounter the same difficulties; some speak of nephritis and others of degeneration. (Nephrosis or tubular nephropathy.) It appears doubtful if this sharp division is expedient since Baehr by suitable dosage of uranium succeeded in establishing glomerulo-nephritis (p. 1318). The consequences of acute nephritis are quite varied. Lighter cases heal in weeks either (1) with permanent loss of some elements (glomeruli) or (2) by restitution to normal, *i.e.*, lost epithelium is replaced by new (Thorel, lit.), and the diseased glomeruli become patulous provided the nephritis had lasted but a few days, and the capillary blood stream has not been completely interrupted, and the exudate and cell masses have been expelled (see Reichel, Lohlein). Other cases become chronic, while still others soon end fatally from edema or uremia. Acute cardiac hypertrophy may develop. (See p. 1356.)

Subacute and Chronic Glomerulo-nephritis Secondary Contracted Kidney. If an acute glomerulo-nephritis fails to heal in about 4 weeks it becomes subacute and then heals, ends fatally, or, without sharp lines of demarkation, enters the chronic stage. During a protracted glomerulonephritis, marked parenchymatous changes develop to such an extent that the macroscopic appearance of the kidney is determined by them. Consequently the term: "chronic parenchymatous nephritis" is often used. But Lohlein pointed out that these cases were in reality characterized by typical glomerular changes, "microscopic glomerulonephritis," and thus we speak of "glomerulo-tubular nephritis." (Aschoff.) Since secondary proliferation of interstitial connective tissue is a natural sequel of destruction of glomeruli and atrophy of tubules, there develop foci of induration during the course of years with progressive contraction of the entire organ. Thus the secondary contracted kidney is formed as the last event in the chronology of glomerulo-nephritis.

The **etiology** corresponds to that of acute glomerulo-nephritis (p. 1333) and the influences of infection, and toxemia are predominant although a certain rôle has always been attributed to exposure to cold and dampness. (Comp. p. 1334.) Sometimes we can demonstrate that a chronic glomerulonephritis followed an acute attack; others are insidious, chronic from the very beginning. The latter appear most frequently during middle life, and usually draw attention by edema of the skin and puffiness of the face.

Clinical Findings.—In subacute and chronic glomerulonephritis the quantity of urine varies but is usually decreased in amount; it is rich in albumen and in the normal solid constituents, dark in color, the specific gravity is somewhat increased, and contains blood at times. The sediment shows numerous hyalin, coarse granular, and waxy casts. Fat droplets and leucocytes are attached to the casts, while frequently there is an abundance of fatty degenerated epithelium, and fatty granule cells. Edema is an important symptom, is usually quite marked, especially in the lower extremities and the scrotum, but occurs also in the serous cavities. As an explanation for nephritic edema, Sahli assumes there is a change in the vessel walls caused by chemically injurious substances. Uremic symptoms are very frequent and death may be due to this toxemia or to edema of the brain, to internal inflammatory processes such as pleuritis, pericarditis, peritonitis, or pneumonia, to gangrene or phlegmon, or erysipelas of the edematous parts.

The clinical symptom complex changes when the secondary contracted kidney is developed; the urine becomes more plentiful, the albumen is less but more than in the true contracted kidney, it becomes lighter in color but is still cloudy, there are many casts, and the specific gravity decreases. The heart hypertrophies according to the degree and duration of the hypertony. (See Lichtwitz.) Edema of the skin, (anasarca), is always present, uremic symptoms are the rule, and frequently there is albuminuric retinitis.

Microscopy in Subacute and Chronic Glomerulo-nephritis, and in Secondary Contracted Kidney.– As soon as a glomerulo-nephritis becomes subacute, the characteristic crescents in the glomeruli attract attention in contrast to the intracapillary changes of the acute stage (see p. 1335) and isolated in the chronic stage. These crescents are proliferations of the loop and capsular epithelium, especially the latter, and cover the skein with a thick cap which may occlude the afferent tubule. Even macroscopically, these changed Malpighian bodies present a striking picture because of their size. We may speak of the extracapillary form of an unhealed glomerulo-nephritis in this connection. But other structures besides the epithelium are seen in the spaces; there are epithelial cells undergoing fatty degeneration, or hyalin droplet formation, hyalin masses of cells, exudates of granular and thread-like coagula, leucocytes and erythrocytes. Intracapillary changes are not wanting and endothelial proliferation may be very noticeable; indeed Herxheimer states that the endothelium may be quadrupled so that the loop is considerably enlarged. In the same kidney may be seen both intracapillary and extracapillary forms of glomerulitis in all degrees. In some scarlet fever cases dying of uremia, the microscopic architecture of the cortex shows no deviation from the normal except for the crescents and the abundance of cells in the large

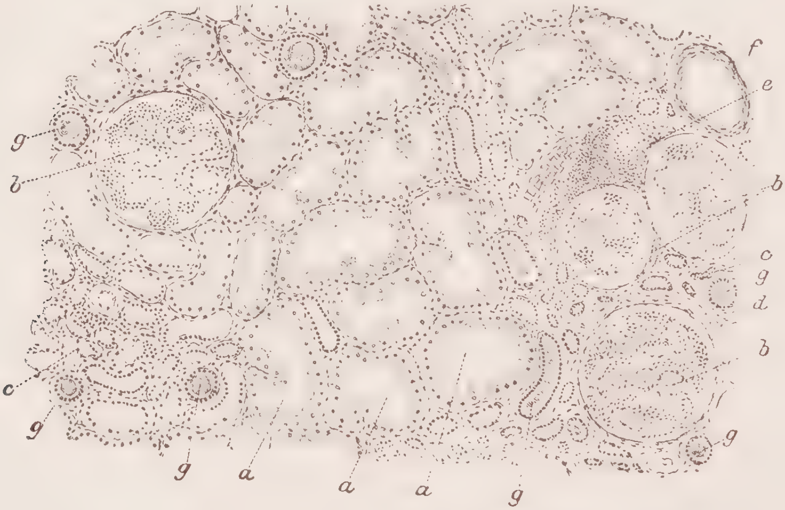


Fig. 699.—Chronic glomerulo-nephritis from a large white kidney, quite smooth on outside. Atrophic induration esp. to right in illustr. a, hypertrophic convoluted tubules, wide with high epithelium; b, some glomeruli, large with hyalin loops, some poorer in cells and shrunken; c, atrophic tubule; d, sclerotic hyalin interstitial tissue; e, small cell infiltration, and to left an artery; f, vein; g, hyalin cast in tubule. (Medium magn.)

glomeruli. The crescents still persist in the secondary contracted kidney, but the further this progresses the more marked the changes in the glomeruli; (*a*) the cells become fewer, and hyalin changes beginning in isolated loops gradually fuse the capillaries to complete atrophy until nothing is left but a hyalin globule, containing but few isolated nuclei or none at all, and intimately connected to a thickened capsule. These hyalin glomeruli sometimes undergo calcification. (*b*) On the other hand, proliferation of connective tissue in the capsular spaces filled by hyalin crescents forms a mass with the skein which eventually becomes hyalinized but it can be distinguished by its concentric layers enclosing the atrophic glomerulus like a shell. (*c*) Focal adhesions between the loop and capsule from which the epithelium is lost make the epithelium which remains have a gland-like appearance. (*d*) Other glomeruli undergo compensatory hypertrophy and are rich in nuclei; they have escaped the acute attack, although in a general sense all the glomeruli are involved, or were only slightly injured and recovered. Their presence is important in understanding the long duration of the disease, for in the chronic stage, different changes are present at the same time and some glomeruli may not be changed at all. In some cases, isolated glomeruli show early stages of glomerulitis while the majority show every form of chronic change, as for instance in the kidney of fig. 702. It does not appear reasonable to assume that the process is continuous from the beginning, it seems more logical to presuppose a reinfection, *e.g.*, with angina, etc.

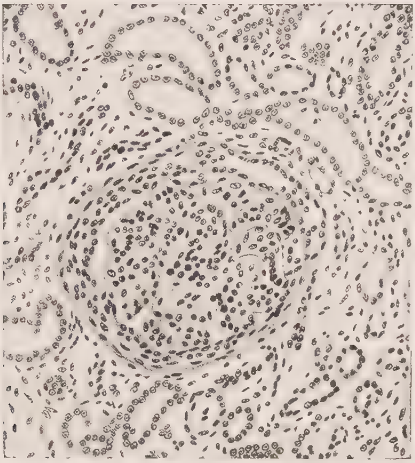


Fig. 700.—From a chronic glomerulonephritis with transition into granular contraction; glomerulus surrounded with crescent; above to right, gland-like space between capsule, loops and two adhesions of loops to capsule; many atrophic tubules, some quite narrow, some wider; interstitial connective tissue broad, partly hyalin; 27 year old gardener. (Med. magn.)

To all this are added degenerative changes in the tubules and the condition was therefore formerly called parenchymatous nephritis; the tubular involvement, however, is often most marked with only moderate glomerular disease. Fatty and fat-like degenerations prevail (see p. 1319), the latter to an exceptional extent in the so-called large white kidney (comp. Stoerk). But as a rule the changes are not as diffuse as the macroscopic picture suggests at first glance, but usually are confined to small groups of tubules about a diseased glomerulus, while tubules in the immediate vicinity are unchanged. (Similar to fig. 684.) The microscope may show that many macroscopic cloudy white spots consist chiefly of collections of doubly refractive fat originating from disintegrated epithelium, and deposited after absorption within the interstitial tissue; such connective tissue cells appear large and clear after extraction of their lipoid contents. (See figs. 686 and 701.) The impression is that the lipoids are lying within lymph vessels (p. 1320). The epithelium of the diseased tubules is swollen, exfoliated, or disintegrated; hydropic (p. 1323) and hyalin droplet degeneration (p. 1323), especially the latter, are very common. Thus an important sequel to the loss of glomerular function is atrophy of the respective tubule, the epithelium of which becomes smaller and the nuclei more intensively stained. The lumena are narrowed and contain various casts, or are collapsed after destruction of the lining cells. The membrana propria is wider and hyalinized. There may even be areas of pronounced atrophy, while the organ is still the large white kidney. When the chronic changes are far advanced, the tubules disappear completely

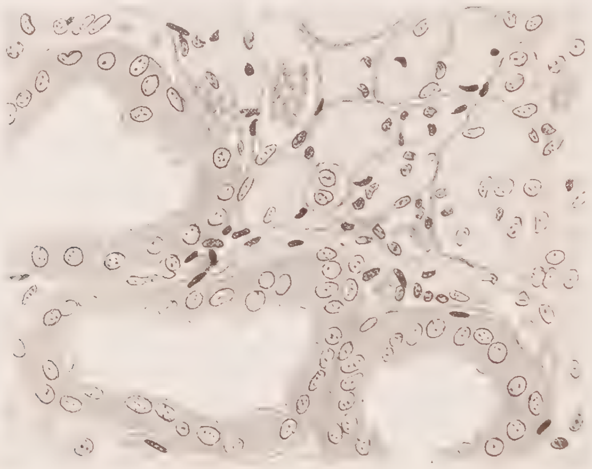


FIG. 701.—Hypertrophic tubules, and in the interstitial tissue between capillaries large finely granular connective tissue cells, perhaps also some lymphatics containing double refracting fat. From the secondary contracted kidney of fig. 700. (High power.)

in some regions and are replaced by connective tissue (see below). The picture is further complicated by the atrophy of glomeruli and their tubules, secondary to the arterial changes so common in chronic nephritis. Frequently the atrophic tubules are distended and contain casts, but the epithelium is small and shows nothing characteristic. Hypertrophic tubules are distinguished by the diameter of their lumen and the size of their relatively well preserved epithelium. (See fig. 701.) Polynuclear cells and isolated giant cells are also found.

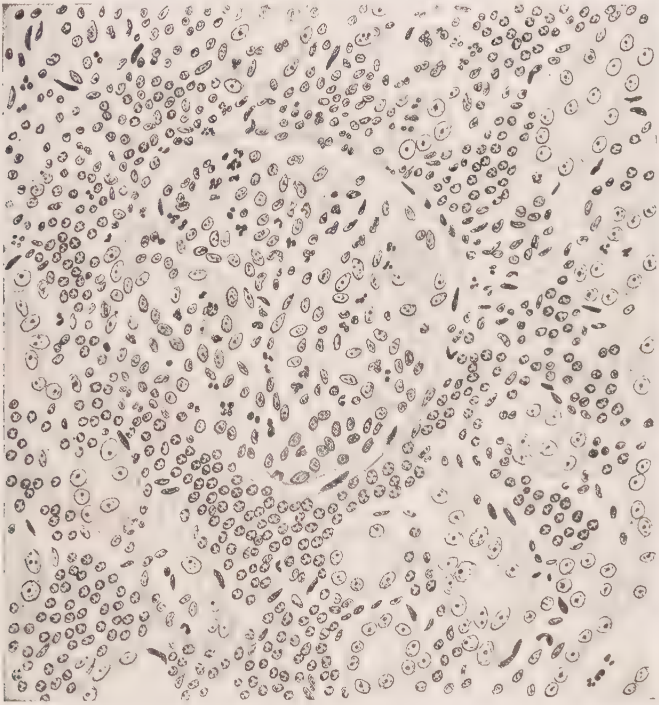


Fig. 702.—Extensive periglomerular and intertubular plasma cell infiltration. The glomerulus shows relatively fresh endocapillary changes. Many others showed crescents and hyalin changes as in chronic glomerulonephritis; macroscopically, large white kidney. In some tubules occasional leucocytes; 20 year old girl; ½ year after pharyngeal diphtheria. (High power.)

Many tubules contain exfoliated, rounded epithelium showing fatty degeneration, or perhaps only debris consisting of fat droplets, necrotic hyalin fusion masses, hyalin droplets of varying, sometimes considerable size, and hyalin casts, the latter especially within the straight tubules of the medulla. Sometimes the tubules contain enough red blood corpuscles to fill the lumen, or they contain granular blood pigment casts. Leukocytes are always found in varying numbers, isolated, fused into casts, enclosed in, or adherent to, hyalin casts. Even calcified casts have been seen.

The interstitial tissue shows inflammatory small cell infiltration, frequently localized to the periglomerular or perivenous regions, or intertubular, especially at the junction of medulla and cortex. These cells are chiefly lymphocytes and plasma cells, the latter sometimes in immense numbers. (See fig. 702.) Leucocytes are also found perhaps within the capsular spaces and tubules. Occasionally there is a small extravasation of blood. In the connective tissue cells lipoid droplets are free or in masses progressing to absorption. (See above.) The connective tissue overgrowth is directly proportional to the number of glomeruli and tubules which disappear; early, there are many round and spindle-shaped cells, but later the cells disappear, hyalinization progresses, and shrinkage takes place as in scar tissue. Even in advanced contraction, however, foci of small cell infiltration remain within the interstitial tissue. When the process is prolonged, the arteries are secondarily involved, the larger vessels showing endarteritic, obliterating and atheromatous changes, the arterioles hyalin thickening and narrowing; this is in the interlobular arteries and the vasa afferentia of the glomeruli as well. These changes of themselves may now cause atrophic processes in the renal parenchyma and thus contribute to the contraction and diminution in size of the organ. Veins may also be thickened.

Macroscopic Types of Subacute and Chronic Glomerulo-nephritis

The Large or Swollen White (or Yellow) Kidney.—The kidney is at least of normal size, usually larger, indeed even two or three times the normal size. As a rule, the larger the size, the softer the consistency. The tensely stretched capsule strips easily and leaves a smooth surface which rarely shows depressions. This surface is pale gray or yellowish white or alternating gray and yellowish white. The striking pallor is due to anemia although isolated venous radicles on the surface may be somewhat congested. On section, the cortex is broadened, often markedly so, and Bertini's cortical columns bulge out from the surface. The color, as on the surface, is diffuse or spotted grayish or yellowish white. Sometimes the broad soft cortex is moist and shiny. Very frequently delicate opaque yellow spots and striae appear on the pale grayish white, somewhat glassy surface, corresponding to groups of urinary tubules undergoing fatty degeneration, (fig. 708), while dull white spots are caused by deposits of a fat-like substance especially in the interstitial tissue. (See p. 1320.) The glomeruli are visible grossly as prominent, pale gray transparent granules. The medulla in contrast to the pale cortex, is usually intensely red (collateral hyperemia) and is often plainly striated.

The Large Red Kidney or Chronic Hemorrhagic Glomerulo-nephritis.—Sometimes white kidneys are encountered with small punctate hemorrhages representing blood-filled capsular spaces or tubule groups larger and perhaps angular, together with scattered red hyperemic striae in the cortex. But we can speak of a large red kidney only if general hyperemia is added to the numerous blood spots and angular red blotches (extravasations) which cause the red color to predominate over the yellow (fatty degeneration) and cloudy white (areas rich in lipoid substance). As a rule, this kidney does not reach the size of the white kidney, and its consistency, if soft, is only slightly so. But not every red kidney is the site of a hemorrhagic glomerulo-nephritis. There are red kidneys without edema and mostly without cardiac hypertrophy as we learned on page 1336, in discussing embolic non-suppurative focal nephritis (Lohlein), but in this complex the enlargement of the organ is not constant as is the large red kidney with edema.

Conditions at the Beginning of Chronic Glomerulo-nephritis; Transition of the Large White or Large Red Kidney into the Secondary Contracted Kidney

If renal insufficiency with general edema and uremia is not fatal the secondary granular contracted kidney develops, even after years. This kidney can usually be easily stripped of its capsule, although at times it is thickened and strips with loss of substance from the bossed surface. The organ is more or less diminished in size although not strikingly so, for the organ was the "large white" or "red" kidney at first and compensatory hypertrophy is often a large factor, especially in children. Occasionally the size is much diminished, *e.g.*, the combined weight of the kidneys of a woman aged 42 who died from uremia was 60 gms. Their surfaces are finely nodular, or more roughly granular, or grained. Protruding areas have a yellow, white yellow, or reddish color. The sunken areas in between correspond to the parenchyma in which sclerosed connective tissue has replaced the normal. This is of dark red to grayish red and light gray color, and may still show minute yellow or white stippling, (lipoid foci or fat debris of tubular epithelium). The nodules and granules correspond to the remaining renal tissue which often contains hypertrophic tubule complexes and perhaps some isolated hypertrophic glomeruli. The light color of the granules is due to their fat or lipoid content and their prominence leads us to deduce a previous large white kidney. Not rarely there are deeply sunken atrophic areas between the nodules and granules corresponding to cicatrized arteries; these continue deeper into the cortex as wedge-shaped scars. On section, the cortex is irregularly decreased in width; gray spots and lines correspond to foci of atrophic induration and deeper scars; the normal architecture of the cortex is thus obliterated and spotted with yellow and gray white foci and striae.

The medullary substance is also atrophic, the pyramids are small and gray spots erase the boundary line between medulla and cortex.

If a secondary contracted kidney originates from a large red kidney—the more frequent occurrence,—the color of the nodules is deeper red and the kidney as a whole more gray red. The alternate red and yellow nodules give a variegated appearance to the organ. (Red contracted kidney.)

If a red color is prominent over the granular surface and the kidney as a whole is indurated, it very nearly resembles the true arteriosclerotic (typical red) contracted kidney (see p. 1352), except for uniformity and fineness of the granules on the surface. Yet the differential diagnosis is occasionally difficult even microscopically, when the arterioles become the deciding factor; we must decide whether all or merely focal groups are diseased, and also whether some isolated glomeruli show characteristic crescents, thus demonstrating glomerulo-nephritis.

Decapsulation.—Edebohl's treatment for chronic nephritis consists of operative stripping of the capsule, but according to experimental findings it has no influence on the nephritis. The capsule quickly reforms from the perirenal tissue, and is usually thicker than before; a more extensive collateral circulation from the surrounding tissue through the newly formed capsule,—the chief aim of Edebohl -does not take place. (Lit. by Herxheimer, Hall, Gatti.) Decapsulation has also been tried in acute renal conditions with anuria, such as in the sublimate, phenol, and eclampsia kidney, etc.; the most frequent result was momentary relief considered due to the removal of capsule pressure on the swollen kidney, (see Rollwage, lit. regarding decapsulation in sublimate kidney), but lasting and curative successes have also been observed. (Luxembourg, Klose in sublimate kidney, see also v. Haberer, lit.)

Others have advised splitting the kidney. Experimentally, severe necrosis of the organ does not follow an exact median longitudinal section through the cortex because the larger arteries are spared. (See Wildbolz.)

True Arteriosclerotic Contracted Kidney.—Herxheimer suggested this name. Other names are: true angiosclerotic contracted kidney, granular atrophy, granular kidney, renal-sclerosis, cirrhosis, atrophy, third stage of Bright's disease, red contracted kidney, vascular nephrosclerosis. The designation "chronic indurative interstitial nephritis" is out of date, and the differentiation between a roughly nodular red granular kidney (secondary contracted kidney) and a finely granular contracted kidney is superfluous.

A complete change of ideas regarding the nature of the true contracted kidney has taken place, *viz.*, that chronic interstitial nephritis induces contraction; today, it is almost universally accepted, as Gull and Sutton, and Jores have stated, that this condition arises from an arteriosclerotic process, but not as in arteriosclerotic atrophic or arteriosclerotic contracted kidneys, (see p. 1312) from arteriosclerosis of larger arteries, but from changes in the arterioles, *i.e.*, in the smallest renal arteries. These are of course coincident with changes in the minute arteries of other organs such as the brain, spleen, pancreas, retina, etc., while others such as those in the muscles remain intact. The essential clinical symptom is hypertony. (Comp. p. 1350.)

We have then a renal disease insidiously developing from a long continued hypertony and characterized by slow progression through many years.

The essential anatomical change consists of chronically developing circumscribed foci of glomerular and tubular atrophy although at times the alterations in the epithelium of the uriniferous tubules seems unimportant,—all depending on changes in the arterioles. It is from these foci that the connective tissue extends by proliferation and accumulates a more or less marked round cell infiltration. This tissue has a tendency to slow cicatricial contraction; conforming to the progressive vascular changes, the process quietly advances step by step until the foci of atrophy lie in an abundant connective tissue containing the glomeruli in various forms and stages of destruction. (Comp. p. 1354.) Closely grouped hyalin glomeruli are especially noticeable and atrophic urinary tubules are still to be seen. (Fig. 704.) But the changes undergone by the arterioles (page 1355) present at the very beginning of the process give the picture its distinctive character. The end result is the granular contracted kidney; where the atrophic areas reach to the surface we find pitted depressions; between them the relatively healthy or even hypertrophic parts of the parenchyma are represented by almost tumor-like protruding nodules. The kidney as a whole is diminished in size, often markedly so.

True contracted kidney is distinguished by marked cardiac as well as aortic hypertrophy, (see p. 1356) to such degrees as are never attained in chronic glomerulonephritis. Functionally this hypertrophy is of great importance.

It is well to remember that there are severe sclerotic atheromatous changes in various other vascular beds, *e.g.*, the coronary arteries, the basal cerebral arteries and their ramifications (see an observation of the author p. 1352) to be viewed as a consequence of hypertonia and regarded as of great clinical importance.

The glomeruli and tubules of the unaffected parts usually show compensatory hypertrophy, and this fact explains that renal function may be sufficient for years, for occasionally even a general enlargement of the kidney is seen notwithstanding microscopic foci of cicatricial atrophy.

A second form of true contracted kidney is recognized by Lichtwitz as developing rather suddenly, especially in young individuals without clear preceding hypertonic symptoms, and leading quickly to renal insufficiency and death from apoplexy, chronic uremia or profuse hemorrhage. The disease rarely lasts into a second year. Anemia and facial edema contrast with the robust appearance of the ordinary hypertony. There are transitions from true typical contracted kidney to this form.

Etiology.—Besides unknown, probably infectious-toxic causes, chronic intoxications must be considered. Severe diffuse arteriole changes progress in chronic lead poisoning (see also Lohlein), and probably some influence affecting unstriped muscle (or its nervous organs) is at work. Metabolic diseases such as obesity, gout, are also held responsible, but the conditions are much more complicated than in lead poisoning. (See Lichtwitz and p. 1376.) Overfeeding is blamed, also alcoholism, excess of smoking and syphilis.

Vascular Hypertony and True Contracted Kidney.—Volhard and Fahr differentiate two forms of "vascular renal scleroses," as they call them, because they say the renal changes are caused by arteriosclerosis, (1) the benign, purely hypertonic, and (2) the malignant. The benign is not dangerous to the kidney while the "malignant" causes severe disturbances of function and leads to advanced contraction. They think the malignant form is caused by an additional something, a new factor, for they believe that inflammation of the loops and cortical parenchyma is essential, and therefore speak of it as a combined form. (See Fahr.) But the latter statement is not believed by Jores, Lohlein, Aschoff and others, who do not consider these inflammatory changes as independent, but as reparative processes. Of course, as a complication, true inflammation, or nephritis may be superimposed upon an arteriosclerotic contraction, (see Lohlein), but this is by no means the rule in the "malignant" form; indeed, the so-called "benign" and "malignant" forms are only differences of degree. The "malignant" is a swiftly progressing form (arteriosclerotic progressive nephrocirrhosis-Lohlein), while the "benign" (the kidney of hypertonia of the clinicians) develops slowly, (initial arteriosclerotic nephrocirrhosis-"lenta"-Lohlein); we might speak of a terminal and an initial phase. The "lenta" is benign with respect to the kidneys which show no severe anatomic and physiologic changes; indeed, we can hardly speak of contraction, because at first it is entirely arteriosclerotic (Herxheimer), with cardiac and vascular symptoms predominant. In fact, when cardiac compensation is diminished in these hypertonic cases the result is far from benign, for sudden and unexpected death from cardiac insufficiency and cerebral apoplexy is quite frequent. The progressive form, on the other hand, is characterized by renal changes (true contracted kidney), and is malignant in the sense of Volhard and Fahr as far as the kidneys are concerned, inasmuch as the symptoms of renal insufficiency predominate, and death is caused by chronic uremia unless, as occasionally happens, a fatal cardiac decompensation or cerebral hemorrhage occurs first.

The Clinical Conditions in General.—As long as the circulation is competent, the urine in hypertonia shows little change, but as soon as cardiac decompensation occurs and the renal changes progress, it is increased in amount, contains but little albumen, is pale light greenish-yellow in color and the specific gravity is diminished; the more urine, the less albumen and the lower the specific gravity. It is quite clear or slightly cloudy, with very little or no sediment and shows but few hyalin casts which are frequently very long and narrow. Epithelium or occasional fat droplets may be attached to them. But few epithelial cells or red and white blood cells are seen; the solid constituents such as urea, uric acid, phosphates, chlorides, etc. are small in amount. Edema is slight or entirely absent as long as there is diuresis and the hypertrophied heart is compensated. Cardiac hypertrophy is practically always present and may be exceptionally great, much more so than with secondary contracted kidney. The pulse is hard, and the increase in arterial tension gives the clinical symptom of "hypertonia," (see p. 1356), present from the beginning and the cause not only of the cardiac hypertrophy, but according to the opinion of many, of the arterio-sclerosis as well. (Essential hypertonia, v. Bergmann.) Albuminuric retinitis develops in the vicinity of the posterior ocular pole around the papilla and macula, together with edema and hemorrhages in all layers of the retina; white spots and striae also appear supposedly due to fatty degeneration. These changes are present more frequently in this than in any other form of renal disease. Indeed examination of the eye grounds is often the first discovery of the basic condition. During the course of the disease, hemorrhages, diarrhea, dyspepsia, and headaches (uremic symptoms) are present. Death may result from cardiac decompensation, from uremia, from cerebral hemorrhage, the latter being quite frequent; apart from the arteriole changes, the kidney may be but slightly altered or a perfect example of the contracted organ.

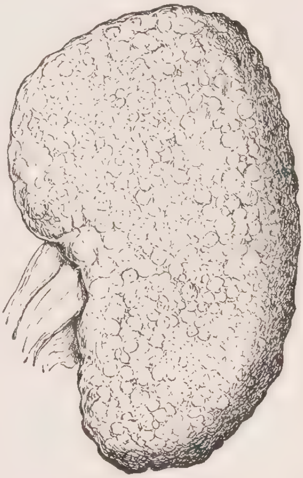


FIG. 703.—True (red) contracted kidney, very severe type, nat. size. True contracted kidneys are often more finely granular.

Deaths from cerebral embolism are rarer. Cerebral hemorrhage may be fatal before other symptoms can be recognized, *i.e.*, the contracted kidney remains latent and the cerebral hemorrhage is the first severe symptom. The author performed an autopsy on a circus dancer 29 years of age, who was apparently quite healthy before an apoplectic attack after a performance; she died soon afterwards. Both contracted kidneys weighed 215 gms; there were advanced sclerosis and dilatation of the basal cerebral arteries. At autopsies in more severe cases, we often find the kidney surrounded with fat to compensate perhaps for the loss of space (so-called capsular lipoma), but the condition is also independent of contracted kidney in lipomatosis. (P. 1311.) The kidney is remarkably small, half the normal size or less, tough and hard; the capsule is adherent, the delicate connective tissue bridges between cortex and capsule are thickened and the capsule itself can be stripped only with loss to the cortical substance. The color of the unevenly granular organ is brown red, red, or red mixed with grayish yellow so that we can differentiate between the red (the more frequent), and the pale granular kidney. Depressions between the nodules are grayish red and consist of vascular connective tissue in which dots can frequently be seen with the naked eye; these are made up of glomeruli lying close together and partly calcified, while the granules themselves consist of relatively healthy, even hypertrophic, parenchyma, similar to the nodules in cirrhosis of the liver (p. 924). On section, the cortex is narrow, perhaps only a few millimeters thick in places. The normal structure has disappeared, and contracted atrophic areas alternate with rounded or oblong islands of soft kidney tissue prominent on the section surface. The pyramids, usually of darker red color, may be relatively large. Arteries are hardened and thickened. Cysts of various sizes are found, the smaller ones quite numerous, the larger ones perhaps of the size of walnuts; they are situated within and on the surface of the kidney. In less advanced stages the kidney may still be firm and large, but its surface is finely granular or grained. Occasionally a true contracted kidney may have a perfectly smooth surface in spite of severe microscopic changes, but the cortex is narrow and its architecture faded. The author saw such an example in a 75 year old man; left kidney weighed 110 gms., the right 120 gms.; the hypertrophied heart weighed 700 gms.; hypertrophy of the epithelium in the well preserved but not distended tubules with numerous giant cells and marked distension of many interlobular capillaries, balanced to a considerable extent the reduction of volume caused by numerous scattered foci of induration. Indeed, not infrequently, the kidneys of certain cases of hypertonia with cardiac hypertrophy are of normal size or enlarged, and merely hard and tough macroscopically; microscopically, however, they show extensive cicatricial atrophy caused by the same changes in the arterioles which occur in the true contracted kidney. The author saw such cases die of cerebral hemorrhage, and Lohlein mentions similar occurrences. It emphasizes that a correct diagnosis cannot always be made macroscopically especially when there is arteriosclerosis of the afferent vessels. The sequence, hypertonia, cardiac hypertrophy, and sudden death from cerebral hemorrhage during perfect health, usually occurs in the third or fourth decade.

Microscopically, the connective tissue foci in the cortex correspond to the macroscopic pitted depressions of the surface; the glomeruli and tubules in these foci show varying degrees of degeneration and simple atrophy. We soon determine that the parenchymatous changes are unimportant in comparison to the interstitial. The atrophic indurated foci prefer locating around the small veins, and in more advanced cases are connected with each other by strands surrounding rounded, oval or elongated islands of parenchyma. The parenchyma itself is not only healthy but often hypertrophic; sooner or later, however, it degenerates and reactive small cell infiltration of the interstitial tissues takes place, as signs that the disease is progressing. As to arterial changes, see p. 1355. But if the non-atrophic parenchyma is more extensively degenerated,

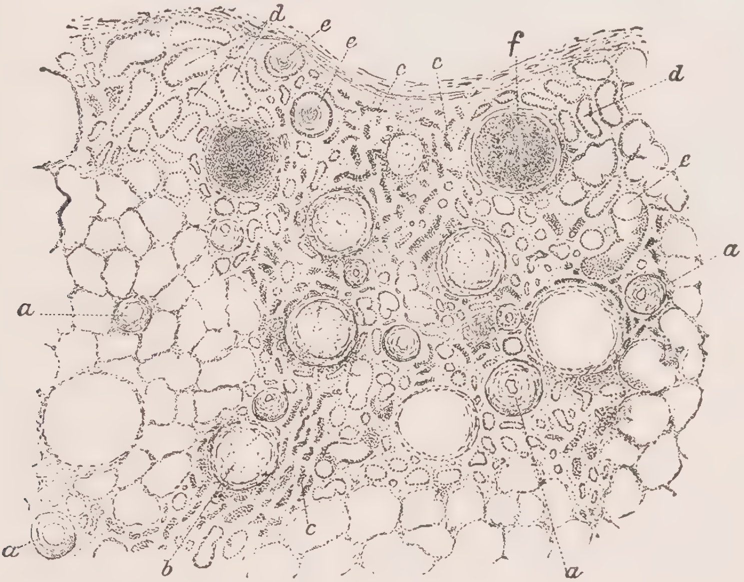


FIG. 704.—True contracted kidney. In center of illustr. an atrophic induration focus within which, in broad connective tissue, mostly poor in nuclei, lie atrophic glomeruli (b), still well preserved (f). Atrophic, in part rudimentary, regenerative newly formed tubules (c); others cystic and dilated rosary-like (e); thickened arteries (a); at d, still unchanged part hypertrophic tubules. The wide meshes in the lateral and lower portions of the illustr. are urinary tubules, the epithelium of which fell out (artefact); three empty capsules of Bowman are present. (Medium magn.)

especially by fatty and lipoid changes, the picture strikingly resembles secondary contraction.

The connective tissue foci show every transition from lymphoid and plasma cell infiltrations to glassy, firm, connective tissue masses poor in nuclei. Even markedly changed areas may still show fresh masses of round cells. Formerly, these pictures were interpreted as diagnostic of chronic interstitial nephritis, but, although Stoerk believes differently, they are now usually considered secondary, *i.e.*, reactive to the irritation of broken down arterioles, glomeruli and tubules. It need scarcely be mentioned that a contracted kidney may be complicated by an independent nephritis and then, of course, the picture is changed.

True Contracted Kidney.—Even within atrophic foci, the glomeruli ordinarily do not show transitional changes, but sharp contrasts between perfect preservation and complete hyalinization, sclerosis and shrinking. The capsules sometimes show slight, sometimes enormous thickening with concentrically deposited hyalin and fibrous connective tissue masses. Many atrophic glomeruli are impregnated with finely granular calcium salts, others appear normal, many are extremely large and rich in cells (hypertrophic); indeed it is quite common to see both extremes as in fig. 705. Lohlein thus catalogues the changes in the glomeruli in the later stages: necrobiosis after collapse of all or portions of the loops subsequent to occlusion; then degeneration and atrophy with the appearance of scars and remnants and debris of the Malpighian bodies; this is followed, on the one hand, by reactive proliferative phenomena, degenerations, lipoid infiltration and cellular invasion, and on the other hand, by more or less retained structure in the loops. The changes remind us of chronic glomerulo-nephritis, and are easily mistaken for inflammation. (Volhard and Fahr; see p. 1350). Lohlein, however, considers the changes in the loops similar to those in the arterioles, and believes it is the tissue destruction which stimulates the reactive inflammatory processes, and thus they are reparatory. Some contracted kidneys show a very marked cellular productive glomerulitis, but this is probably secondary. Here and there the uriniferous tubules are either quite destroyed, collapsed, or narrowed to small clefts, or are smaller and lined with low cubical epithelium. Many contain casts, often in great numbers. In many places the atrophic tubules are surrounded by hyalin sclerotic connective tissue as by glassy rings. Some tubules are cystic and dilated by the retention of secretions or urine; others show compensatory hypertrophy, and large epithelial cells lining dilated lumena are encountered everywhere (fig. 704). Other tubules have large epithelial cells, narrow lumena, and fairly numerous cells with two and even many nuclei (giant cells). Regenerative new formation of true urinary tubules does not take place, (see Thorel, Sacerdote; also p. 1328). It is interesting to remember that regeneration can exceed the limit and cause the development of small adenomata. The blood vessels within atrophic foci react in the following way: some of the capillaries within the foci break down completely; other interlobular capillaries become markedly distended, (red color of kidney). Atrophy of larger amounts of the cortex is followed by enlargement of the medullary vessels. According to Prym and Jores, the changes in the arterioles are similar to those of ordinary arteriosclerosis and are characterized by both degenerative processes, (fat stained with sudan), and hyperplastic thickening of the internal elastic layer (Jores). The whole wall may undergo hyalin change, and Hueck believes that this hyalin degeneration is the deciding characteristic of the arterial change, and thinks it consists of penetration of the wall from within outward by a substance which at the beginning is soft or semiliquid, and that fatty degeneration is an accident and may be completely absent. On the other hand, Lohlein speaks of atherosclerosis and describes the changes in a contracted kidney as follows: at first circumscribed hyalin granules, clumps and rings appear below the endothelium, which steadily increase in size and become infiltrated with lipoid substances and occasionally encrusted with lime salts, while more rarely, at the beginning, considerable cell proliferation of the wall occurs, which is also gradually infiltrated with lipoids. Again according to Lohlein, complete atherosclerosis of the arterioles decides the pathogenesis of true contracted kidney, for he did not find atherosclerosis of the arteri-

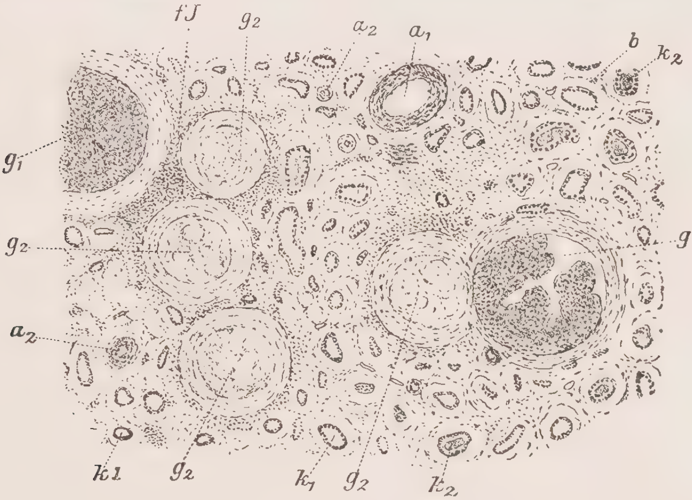


FIG. 705.—True contracted kidney; a-1, larger thickened artery; a-2, one of the numerous thickened narrow arterioles; b, connective tissue markedly broadened; fj, fresh infiltration focus; g-1, glomeruli with hypertrophic loops and thickened capsules; g-2, obliterated glomeruli; the hyalin loops fused with the thickened capsule; k-1, one of the many atrophic tubules; k-2, atrophic tubules with casts. (Med. magn.)

oles in simple hypertony, but rather a dilatation exclusively of all the vasa afferentia with more or less sclerosis of the stretched vessel walls, which he designates as "early sclerotic." Injuries to loops and tubules are usually absent. Herxheimer saw hyalin fatty thickening of the intima in advanced hypertony, even if the kidneys were still unchanged macroscopically. According to Ewald, Friedemann, there occur cases of pure muscular hypertrophy which may be considered as part of the hypertrophy involving vessels and the left heart, but Jores is sceptical of this view since errors may have induced it, (rigor mortis, etc.). Gaskell too saw marked general hypertrophy of the larger renal arteries.

The arteriosclerosis in true contracted kidney has aroused much controversy. Gull and Sutton believe it is the essential factor in the cause of contracted kidney, but they go too far when they assume that this vascular change involves all parts of the body (Fahr). Jores, who emphasizes the degenerative and obliterating changes in the afferent vessels, considers it a result of cardiac hypertrophy, the chronic course of which permitted the contracted kidney—then considered as chronic interstitial nephritis—to develop, and wearing out processes lead secondarily to sclerosis of the renal arteries, (Lohlein and others). This latter opinion is not accepted today, but the mere fact that arteriosclerosis is found in the very beginning of contracted kidney and that the hypertrophy of the heart is already developed when changes are beginning in the kidney, seem to speak for independence of the cardiac hypertrophy and the arteriole changes in the kidneys and certain other organs, such as the spleen, brain, pancreas, liver, while in still others, such as, body musculature, there are no changes. (Jores, Fahr.) The changes as a whole can therefore be considered due to blood pressure increase, (hypertony), consequent to some factor as yet unknown, (see below), exactly as is the cardiac hypertrophy. But then the usual left sided cardiac hypertrophy has been explained in various ways, (lit. Paessler); its presence is undoubted in most forms of chronic nephritis, (exception p. 1347), even after a glomerulo-nephritis of only 4 weeks duration; it is especially marked in true contracted kidney with its precursor, simple renal arteriosclerosis. (P. 1347.) The "pressure theory" assumes that the hypertrophy develops from the resistance offered by the vessels in atrophic areas scattered through the contracting kidneys, and in spite of the fact that these areas are apparently small, the idea gains ground when we consider the large quantities of substances excreted by the normal kidney, *i.e.*, the large amount of blood passing through them. It also appears quite possible from certain experimental investigations, (see Passler and Heineke, Katzenstein, lit., Fahr, lit.). Volhard thinks, with Bier, that when the function of numerous glomeruli is abolished, the reduced filtration surface requires a compensatory increase of filtration pressure, *i.e.*, increase of blood pressure with its cardiac hypertrophy. But we often see hypertony with types of renal disease without marked glomerular participation. The increased resistance in many renal vessels might cause hypertony and cardiac hypertrophy, but it is still a disputed question whether the anatomical vascular change, demonstrable, according to Munzer, throughout the entire precapillary peripheral arterial system, is primary or is secondary to hypertony. According to the opinion of many, blood pressure increase always causes abnormal contraction of arterioles over extensive areas, and can be induced by various factors which are only partly understood, (Lohlein); to mention a few: nervous disturbances in the emotional life through certain of the sympathetics (v. Monakow), toxic substances such as lead, lues, gout, internal secretions with factors influencing the vasomotor centres (see Pal, v. Bergmann); this shows that hypertony is a symptom without uniform etiology. Renal arteriosclerosis is presented as a consequence of hypertony of some duration. (See also Hueck.) Lichtwitz expresses the thought that changes in the renal vessel walls may initiate a nervous reflex (see M.B. Schmidt), which stimulates extensive vascular areas of the body to contraction and thus produces hypertony with consequent cardiac hypertrophy.

The theory of "chemical irritation" assumes that the blood, contaminated by urinary products, exerts an irritative "pressor" contracting influence on heart and vessels, thereby raising the blood pressure and leading to cardiac and arterial hypertrophy. The constantly increased tension causes the arteriosclerosis. Jores believes that the reason for marked cardiac hypertrophy in red granular kidney is not basically the renal disease, but the same injury which caused the granular kidney through increase of blood pressure. Ceelen supposes it is due to toxic effects on the ganglion cells of the vasomotor centre which are chronically irritated. Wiesel and Schur point to the frequent coincidence of cardiac hypertrophy and enlargement of the adrenals with an analogous increase of all chromaffin substances in the whole chromaffin system, (p. 1277); furthermore, they demonstrated that the blood serum of nephritics possesses a mydriatic action similar to adrenalin (pupillary enlargement in the eye of the frog), and they assume there is a correlation between cardiac hypertrophy and the chromaffin system, the function of which is influenced by renal changes. Bittorf, Oberndorfer, Goldschmidt and others, however, could find no definite relation between medullary hypertrophy and cardio-renal-vascular disease; nevertheless, Nowicki believes in increased adrenal activity in chronic renal diseases and correlates the vascular changes in this way. (See Aubertin, Clunet.)

Involvement of the cerebral arteries, which makes them subject to easy rupture, plus cardiac hypertrophy with its blood pressure increase explain the frequency of cerebral hemorrhage in true contracted kidney, (p. 1351). It must not be forgotten that there are cases of contracted kidney in marasmic individuals in whom no cardiac hypertrophy develops, or if present at one time, has partly receded. (See F. Muller, Marchand, Lubarsch, Wideroe, Fahr.) [Major and Stephenson, and Major discuss guanidine compounds as possible factors in the production of high blood pressure. For discussion and lit. see their papers: J. Hop. Hosp. Bull., 35: 186: 1924, ibid. 35: 140: 1924; J. A. M. A. 83: 81: 1924; ibid. 85: 251: 1925; Am. J. Med. Sci., 170: 228: 1925.—*Translator.*]

Cardiac hypertrophy causes increase of arterial pressure and increased excretion of urine. The latter process is made possible by the vascular conditions mentioned on p. 1313, in spite of the impermeability of numerous glomeruli (Thoma). If the compensatory hypertrophy of the left ventricle fails, or if the renal parenchyma becomes ineffective and the vicarious eliminators of urea (bowel and skin) also fail, uremia appears as an intoxication of the body by retained urinary substances which apparently cause vessel spasm, especially in the brain and spinal cord. With sudden failure of cardiac compensation, a possible latent renal disease may be ushered in by uremia with sudden death as a result. In gradually failing cardiac compensation, we see disturbances of the venous circulation, with edema and marasmus; death may follow from complications such as inflammation of serous membranes, pneumonia, endocarditis etc., (for uremic skin diseases, see Chiari, Gruber). [For review of experimental acute nephritis see MacNider, W. DeB., Physiol. Rev. 4: 595: 1924. For methods of producing chronic nephritis in animals, functional studies, x-ray damage, etc., see Hartman, F. W., Bolliger, A., Doub, H. P., Am. J. Med. Sci., 172: 487: 1926, Radiology, 8: 142: 1927. J. A. M. A., 88: 139: 1927. Ann. Clin. Med. 7: 599: 1927.—*Translator.*]

So-called Amyloid Degeneration (Amyloid Infiltration) of the Kidney. Amyloid degeneration is the infiltration of certain parts of the vascular connective tissue apparatus with a glassy substance which stains brown with an iodine solution, and is part of the symptom complex of general amyloidosis. (See p. 947.) It involves intestines, spleen, liver, etc., or perhaps only the kidneys.

Microscopically, the glomeruli are usually affected first, naturally to varying extents, but in other cases, the vasa recta of the medullary substance are either alone or chiefly diseased. In the glomeruli, one loop after another undergoes glassy change.

According to Hueter, the amyloid is excreted after exfoliation of the endothelium to the internal surface of the capillaries, but all the loops finally change to glassy, lumpy, enlarged masses impermeable to blood. The epithelium of the glomeruli may persist for some time but disappears later via fatty degeneration. Then the afferent vessels and the straight arterioles are attacked, and finally all arterial, venous and capillary vessels, especially of the cortex, so that the lumena of the vessels are narrowed or obliterated. Then follows the membrana propria of the uriniferous tubules, especially of those in the medulla.

All amyloid tissue takes a mahogany brown color with iodine. (Reactions under liver, p. 948.) Slight degrees without changes in epithelium, interstitial tissue, or glomeruli but with involvement of the vasa recta, cause no clinical symptoms. (Rosenstein and others.)

More marked degrees are frequently combined with degeneration in the tubular epithelium and the condition is presented as a renal degeneration, ("nephrosis;" also called at one time, parenchymatous nephritis), with amyloid infiltration of the vascular connective tissue apparatus. Probably both changes are due essentially to the same injuries, but the degeneration may be partly a result of insufficient blood supply, *i.e.*, a consequence of amyloid. Among the degenerations, the hyalin droplet, fatty and lipoid types predominate. The tubular epithelium, especially that of the most sensitive parts, the convoluted tubules, is most severly affected. Fatty detached cells produce epithelial or granular casts, and fat and fat-like substances are almost always present in the interstitial tissue, (p. 1320). We find albumen in the capsular spaces, and frequently large numbers of hyalin and waxy casts in the uriniferous tubules. These casts stain bright yellow with iodine, (rarely brown as amyloid).

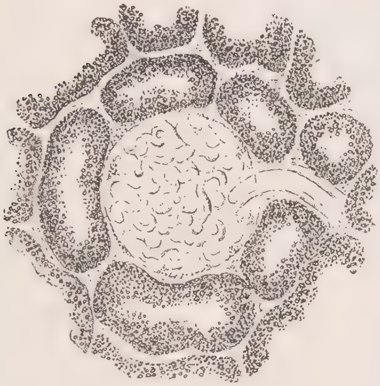


FIG. 706.

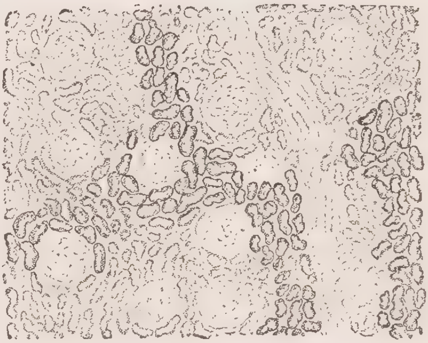


FIG. 707.

FIG. 706.—Large white amyloid kidney; amyloid glomerulus with amyloid in afferent vessel and traces of fatty degenerated epithelium surrounded by convoluted tubules with marked fatty degeneration of epithelium. Minute fat granules in interstitial tissue. Fresh unstained section. (High power.)

FIG. 707.—Large white amyloid kidney; light amyloid glomeruli; spotted fatty degeneration of tubules; other tubules show cloudy swelling. Fresh unstained section. (Low power.)

An inflammatory reaction in the connective tissue between the uriniferous tubules takes the form of small cell infiltration; it is probably secondary to epithelial destruction. There are also cases in which amyloid degeneration succeeds nephritis of some duration, and then cardiac hypertrophy develops. (Lit. by Raubitschek.)

In milder degrees, usually nothing remarkable can be seen macroscopically. In more advanced cases with hyalin droplet and fatty degeneration of the epithelium, the kidney becomes the so-called large white amyloid kidney (Litten). It is large, firm, heavy, (300–400 gm.), the capsule strips easily, the surface is pale and smooth, the venous rays are frequently injected in spots. The medulla and cortex are sharply differentiated, the medullary substance is usually light or dark red (hortensia red). The broadened cortex and the broad columns of Bertini are pale gray, and the anemia and fatty and lipoid degeneration add yellow and white spots. The gray areas are transparent, dry, waxy, with a dull sheen; the yellow and white spots are opaque. If the epithelium is less degenerated, the color is pale gray, (bacony and waxy kidney). Dewdrop dots in the cortex (glomeruli) and delicate striae corresponding to the amyloid vessels and amyloid membrana propriae of the tubules of the medullary substance will stain brown on treatment with iodine.

The severe local circulatory disturbances often cause thrombosis of branches of renal veins and the white or pale red thrombi can be seen protruding from the veins on the section surface. Thrombosis may continue into the trunk of the renal vein and even into the cava.

In time, (sometimes years), numerous groups of tubules are destroyed and the glomeruli are crowded together forming contraction foci within which the fibrous connective tissue is increased and small cells accumulate. The kidney is quite firm, irregularly lobulated, granular, and smaller, (amyloid contracted kidney).

In this condition cardiac hypertrophy and increased blood pressure are usually absent, since it occurs mostly in anemic and cachectic individuals (see exception above); actually the heart may show brown atrophy. But uremia may develop, although death is usually due to the cachexia of the underlying disease. The urine in amyloid kidney may be practically normal in quantity, or decreased, or increased, (as in amyloid contracted kidney, see Munk.) The color is pale yellow, it is clear, the specific gravity is normal, decreased or increased. Albumen may be absent, but usually is abundant (1–2%); sediment is absent, but in more severe degrees it becomes abundant and morphological elements are present in quantity. Usually, casts (page 1326) (hyalin, waxy, granular), as well as leucocytes, are scarce. Edema is considerable but may be absent. Retinitis is generally absent. As a whole, the most suggestive signs are a markedly increased amount of urine with abundant albumen, no increase in blood pressure or cardiac hypertrophy and enlargement of both the spleen and liver. (Leo, "Diagnosis.") The most important point is due consideration of the basic disease; there is no direct clinical sign of amyloid kidney. (See Munk.) (Lit., esp. of experimental amyloid kidney, by Braut and Courcoux.)

Suppurative Nephritis

Two main types must be differentiated in interstitial suppurative inflammation of the kidney with abscess formation due to invasion by pyogenic organisms: (*a*) hematogenous or metastatic, descending; the pathogenic organisms reach the kidney via the arterial blood stream and lie at first in the vessels: (*b*) by continuity, ascending from the lower urinary tract to the pelvis and from there to the collecting tubules. On account of its origin, the latter form is called pyelonephritis.

Hematogenous or Metastatic Suppurative Nephritis.—We speak of renal carbuncle when a metastatic staphylococcus infection appears in the kidney after a furuncle, not in the form of multiple foci, but as a tumor-like infection progressive in character (Barth). In severe infections such as septic endocarditis, pyogenic wound infections, furunculosis, carbuncles, scarlet fever, diphtheria, puerperal infection, etc., pyogenic organisms reach the kidney via the blood stream; they are usually streptococci or staphylococci. They may be numerous enough to plug the capillaries (capillary embolism). The involvement is usually bilateral, but not without exception, and multiple; more or less numerous, or innumerable rounded foci (abscesses) appear chiefly in the cortex. They are miliary or as large as a pin-head, rarely the size of a pea, soft, yellowish and prominent, often surrounded by a more or less broad red zone. There may also be multiple punctate hemorrhages. When the capsule is stripped, superficial abscesses are torn, and if the capsule itself is invaded it may be torn when stripped. On section the medulla shows elongated striped abscesses and the cortex rounded abscesses, but in the cortex also there may appear striae or rosary-like foci corresponding to the medullary rays; these are excretion foci, (see below). Sometimes there is wedge-shaped septic infarction, and the necrotic tissue is surrounded by a broad zone of leucocytes. Microscopically, the rounded cortical foci show glomerular loops plugged with bacteria, or bacteria-containing intertubular capillaries which become convoluted and varicose and finally necrotic. At first the bacterial clumps are surrounded by "toxin zones" of various widths, within which all nuclei are lost and no leucocytes are to be seen. Peripheral to the necrotic zone are masses of leucocytes which overflow into the surrounding tissues. A reactive inflammation begins in the neighborhood and round cells enter the connective tissue and tubules; the epithelium of the latter undergoes granular and fatty degeneration, and the connective tissue likewise disintegrates. Thus, when the focus is permeated with pus cells and the connective tissue has broken down, a true abscess is formed. But these foci do not always become abscesses; the tubules and the glomeruli may atrophy and contract, and wedge-shaped atrophic foci result within which are hyalin glomeruli and connective tissue infiltrated with small cells.

The oblong suppurating medullary foci form in two ways. (*a*) Rarely, they follow groups of cocci in the blood vessels in which case they are similar to the rounded cortical foci. (*b*) Usually, they develop in this manner: bacteria enter the capsular space and thus are washed onward in the tubules, (excreted); they are then obstructed in their progress perhaps by casts in the middle and central portions of the medullary cones, *i.e.*, in the loops of Henle and the collecting tubules (bacterial infarcts); possibly the casts serve as pabulum; finally necrosis and abscess formation are the results, (excretion foci, Orth). The bacteria thus lie within the uriniferous tubules glued to hyalin casts or actually forming casts themselves. Necrosis begins around the bacterial clumps which are densely surrounded by leucocytes; they, with the products of the disintegrated renal tissue, constitute the abscess. But some of the bacteria may be expelled and excreted in the urine. The elongated medullary foci may be found with rounded cortical foci or without them. Orth calls the latter condition, "metastatic medullary nephritis," and in such cases the organisms pass the glomeruli and produce pus only in the medulla. In animals J. Koch (lit.) succeeded in producing changes only in the medullary substance by injections of weakened cultures of staphylococci into the circulation.

If the bacteria accumulate in the papillary points, they show brown striations and may become completely necrotic; this is spoken of as papillary bacterial nephritis, (Orth, see also pages 1364 and 1405). (See Rolly for the ready permeability of the normal and the diseased kidney for bacteria.)

Suppurative Nephritis by Continuity. Pyelonephritis.—We may also use the name "ascending pyelonephritis" when the infection ascends from the urethra or bladder, in contradistinction to the (rare) descending form in which inflammation progresses from the kidney to the pelvis.

This is more frequent than the metastatic type and the changes are far more impressive, even though they may be unilateral. Stasis, and the decomposition of urine accompanying cystitis, are often its forerunners. The causes of retention of urine are many: there may be changes in the urethra such as prostatic enlargement and tumors; in the bladder such as inflammations, calculi, tumors, and especially paralysis; in the ureter such as kinking, calculi and external constricting tumors of the uterus, and in the pelvis itself such as calculi, and tumors. The organisms concerned are chiefly, although not exclusively, (see Roman), bacteria of the colon group (see, among others, O. Hess). They reach the pelvis from stagnant urine through the ureter and cause pyelitis; from there they enter the collecting tubules and ascend to the uriniferous tubules, but first fill the medullary tubules and may form actual casts. Necrosis, fatty degeneration, and pus cell infiltration follow and thus an abscess is developed.

Recently, there has been a tendency to attribute more frequency to the hematogenous route of infection in pyelonephritis than to the urinogenous route, (Kapsammer and others). There have also been doubts expressed as to the possibility of urinogenous infection ascending into the uriniferous tubules. Thus, A. Muller (lit.) considers the lymph channels the most important means of transmitting infections from the pelvis to the parenchyma, (see also O. Hess). Invasion of all kidney levels may occur in this manner. Ribbert believes toxins from the medullary apices reach the interstitial tissue by absorption and lead to heaping up of leucocytes in the capillaries and veins; bacteria do not enter the straight tubules but pass from the papillary points to the veins and from these into the adjacent tubules; within the tubular system they reach the cortex and medulla in the urinary stream.

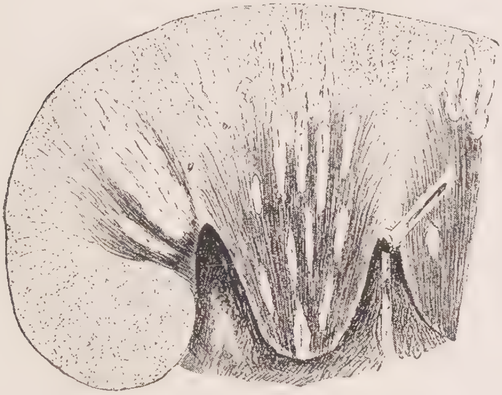


Fig. 708.

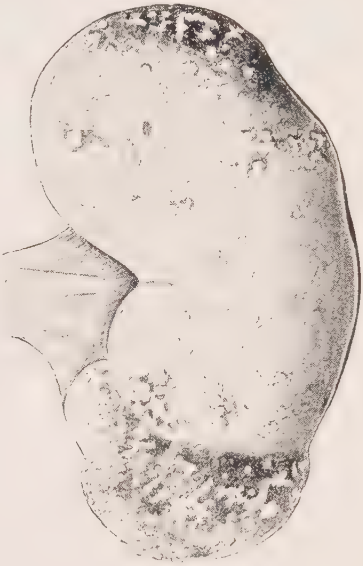


Fig. 709.

Fig. 708.—Ascending pyelonephritis; portion of main section of kidney; ascending abscesses in medulla and cortex; inflammation in interstitial tissue; parenchymatous degeneration of cortex; cystitis and hypertrophy of prostate; nat. size.

Fig. 709.—Kidney with pyelonephritis, external view. Numerous small abscesses, often in groups with hyperemic zones; here and there punctate hemorrhages. At both poles swelling around dense abscesses and diffuse hemorrhages between foci; drawn from fresh specimen; $3/5$ nat. size.

The pyelonephritis of pregnancy or the puerperium is often only a pyelitis without renal involvement, and according to Opitz (lit.), is almost always an ascending colon bacillus infection with its origin in the bladder. (See Ruppanner, lit., Kehrer, Engelhorn, Gustafson, lit.) It is more frequent on the right side and may be favored by pressure of the pregnant uterus on the ureter. But according to Hicks, the pyelitis of pregnancy, and this holds true for the pyelitis of all women and children, is initiated by invasion of colon bacilli from the bowel by means of the lymph channels to the pelvis, while the lower urinary tract escapes. Others, (for instance, Bumm), assume it is hematogenous following digestive disturbances, constipation, etc. Still others believe that a hematogenous origin has not been excluded, for instance, in angina. (See Franz, Doderlein.) In reference to the cystopyelitis in children, ascending from the urethra, as well as defloration pyelitis, see under pelvis, p. 1417.

During inflammation of the pelvis and the kidneys in connection with calculi, bacteria reach the pelvis by the ascending route, or by way of the blood after passage through the kidneys, or by the lymph channels in the vicinity, (the intestines). Further invasion of the bacteria into the renal substance progresses in the above narrated manner. In suppurative nephritis following non-penetrating trauma we must believe that, given a point of lowered resistance, bacteria find their way about in a similar manner.

Abscesses appear in the medullary substance in great numbers as isolated or confluent swellings and as striae of varying thickness which continue from the medullary substance either directly or with interruptions through the cortex to the surface. Here they appear as slightly bulging yellowish soft dots usually of small size, isolated, or united to branching foci, or as confluent groups the size of a dime or larger. They are often surrounded by red zones. Where the abscesses are crowded together, the kidney tissue is soft, swollen, cloudy, pale, or is filled by hemorrhages; sometimes it is necrotic and clay-colored. Small abscesses are enlarged by confluence.

The several medullary cones are involved in varying degree; frequently only a few, rarely but one, will show changes.

"Diphtheria" or Necrosis of the Papillae.—Sometimes the papillae become necrotic at their apices which are then covered by a gray scab. When necrosis is complete the papillae become glassy, as though cleared in oil, greenish gray or brown, remarkably dry, tough and shrunken; they may become detached and even occlude the ureter. Microscopically, the collecting tubules are thickly packed with bacteria; the necrosis is doubtless the result of intensive action of bacterial toxins, (see hydronephrosis, p. 1405).

The course of the disease. The abscesses and infiltrations may heal with scar formation, and the kidney surface exhibits large numbers of pitted retractions to which the capsule is adherent. Healing may take place in one area, however, while the inflammation progresses in another, (chronic purulent nephritis). Such cases are met fairly frequently. Rarely, a larger abscess is found encapsulated by connective tissue, or a cicatricial focus will contain a residue of thick pus with calcareous, fatty and caseous granules, (mistaken for tuberculosis).

Through confluence, larger abscesses are developed and perhaps break into the pelvis leaving an ulcerating cavity at the point of rupture. Finally as the loss of parenchyma is completed, the whole kidney becomes a pus sac (pyonephrosis), the wall of which is formed by the proliferated, thickened fibrous capsule. If the contents escape in any direction the sac shrinks until it eventually becomes a small connective tissue mass in which are sometimes retained irregular remnants of the pelvis and caseous or calcified pus collections, (mistaken for tuberculosis). If the capsule is perforated, the suppurative perinephritis may continue in the perirenal fat and beyond, (fat, connective tissue and even musculature), as a paranephritic abscess, to finally penetrate the external skin or the bowel, abdominal or pleural cavities, (p. 1420). Peri- and paranephritic abscesses of longer duration cause considerable cicatricial thickening of the capsular tissue. Pyelonephritis may also lead to pyemia by invasion of the circulation (V. Wunschheim). The author saw pyemia caused by a purulent thrombophlebitis extending by continuity to the vena cava.

Specific Inflammations

Renal Tuberculosis.—Tuberculosis of the kidney appears in various forms: A, as secondary, metastatic, hematogenous miliary tuberculosis. Miliary nodules appear as part of a general acute miliary tuberculosis, or isolated, as discrete tubercles in chronic tuberculosis, especially of the lungs. In the first type, both kidneys, especially the cortices are thickly studded with nodules. Bacilli reach the kidneys via the blood current, are caught in the glomeruli or narrow cortical and medullary vessels, and either remain there provoking the formation of rounded tubercles, or escape through the glomeruli and are carried by the urine into the medullary parts; here they may be halted, especially in the straight tubules, where they cause tubercle formation (excretion tuberculosis, Orth), often in elongated shapes. As stated, in general miliary tuberculosis, the nodules are more numerous in the cortex, although the medulla does not usually escape; in a few cases the process is confined to the region of a single arterial branch. They appear on the surface as washed out, gray-white, flat spots often numerous enough to cover the surfaces of both kidneys like an exanthem. They sometimes have punctate cloudy yellow centres, or, if older, bulge slightly and are white or yellow without sharply marked borders; at times, there is a red peripheral zone, whereupon the nodules may be mistaken for small abscesses. On cross section of the kidney, the tubercles are washed out spots, mostly opaque in the center and gray-white in color, or nodules more sharply outlined, rounded and caseating. Others appear as tiny wedges and striae, following like a string of beads the course of the ascending arterioles or medullary rays

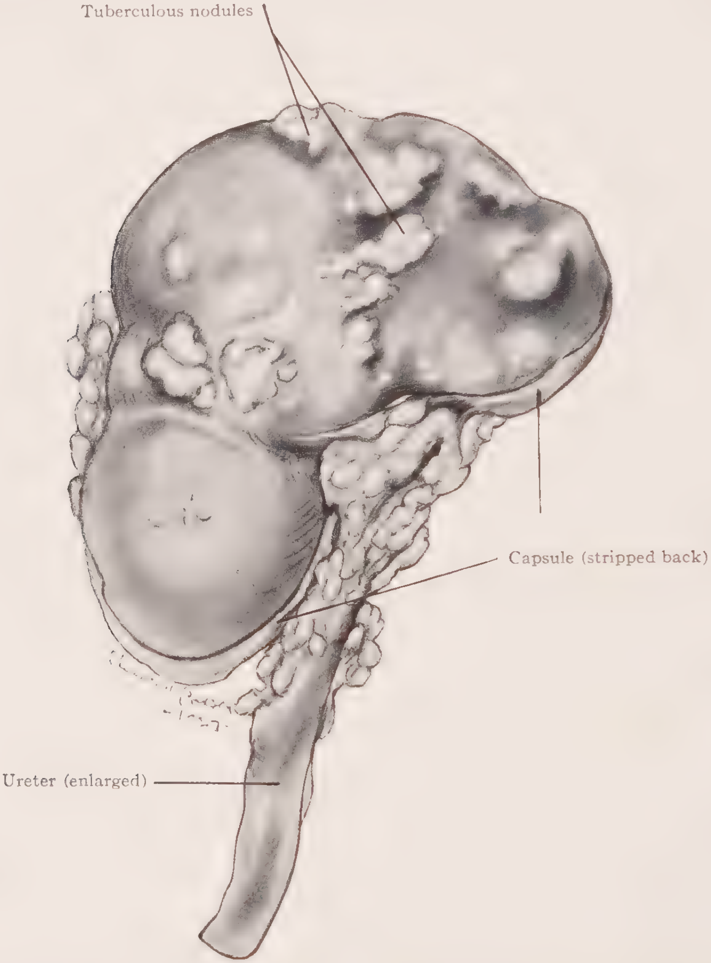


Fig. 710.—Tuberculosis of the left kidney. Surgical specimen. The type tuberculosis in this case was that of large caseous nodules, the caseation remaining quite stiff, tough and firm. On section the calices were destroyed. The other kidney, according to cystoscopic evidence, was normal. Patient made an uninterrupted recovery and has remained well for 4 years. In our experience results of the removal of kidneys are eminently satisfactory in this condition except in comparatively late stages when bladder, etc. are extensively involved. L. H. #734.

and reaching as far in the medulla as the papillary apices. The latter appearance points to infection of the afferent tubules (excretion tuberculosis). Miliary tubercles may be scattered in the pelvis.

Miliary tuberculosis of the kidneys is often a latent disease; in individuals with chronic pulmonary tuberculosis W. Fischer found specific tubercle formation in the kidney in over one-half of the cases, though usually in slight degrees. He could not verify the presence of a real tuberculous nephritis.

Microscopically, the gray-white spots are cellular infiltrations into the connective tissue, and may enclose isolated urinary tubules with their epithelium undergoing cloudy swelling, fatty degeneration and necrosis. They are often grouped around small vessels or a caseating glomerulus, or are attached on, or around glomeruli, the epithelium of which, like that of the tubules, assists in building up the tubercle by proliferation and, at times, by the formation of giant cells. But the chief factor in tubercle formation is the interstitial tissue. The formation of tubercles in arterial walls may lead to occlusion and subsequent focal atrophy or to frank infarcts, anemic, or more rarely, hemorrhagic, (Orth). In this way granular kidneys are developed, (tuberculous contracted kidney; see also p. 1370). Dissemination of tubercle bacilli may also be observed within the area supplied by a tuberculous artery, thus causing a kind of tuberculous infarct, (D. Nasse).

Borrel, Friedrich and Noesske produced renal tuberculosis experimentally by injecting tubercle bacillus cultures into the arterial blood. Asch also succeeded by direct introduction into the renal artery. Buday studied the histogenesis of the renal tubercle. See Meinertz's investigations under modified conditions, and Pels Leusden, who produced local isolated renal tuberculosis by injections into the artery.

Chronic local tuberculosis shows two chief forms: the one most important and most common, is the caseous-cavernous form in which caseous foci become necrotic cavities with perhaps no intercommunications, but direct connections with the tuberculous pelvis, (tuberculous pyelonephritis). Its pathogenesis may be as follows: probably most frequently, the bacilli reach some area in the kidney via the circulation and provoke the formation of an elongated or rounded tubercle, often in the medulla, but sometimes at the boundary between medulla and cortex. The focus extends *en masse* within the parenchyma until it reaches the size of a pea, when it becomes caseous and softens within to a cavity. It may remain completely encapsulated (closed tuberculosis), although occasional bacilli pass into the tubules and reach the pelvis, or it may rupture into the pelvis (open tuberculosis) and extend toward the cortex at the same time. Thus in the early stages, only a small area of the pelvis is covered with nodules or is caseous and ulcerated. From here the process attacks papillae, calices and progressively larger parts of the parenchyma, as nodules in chains or stripes extend far into the healthy tissue. This type is more frequently unilateral, at least for a long time, (see Swan, Frank, Wildbolz). If the lower tract is infected from the kidney, (ureters, bladder, prostate), it is called a descending urogenital tuberculosis.

Wegelin and Wildbolz (lit.) in operative cases, mostly on individuals in the 3rd decade, found that the lateral planes of the medullary pyramids and the neighboring calices were affected. Ekekorn points out, as Pels Leusden had done before, that in primary hematogenous renal tuberculosis the infection of the pyramids and calices may be secondarily ascending from the pelvis.

In the other type, the caseous-cavernous form develops as an ascending pyelonephritis, *i.e.*, secondarily from the pelvis in tuberculosis of the extrarenal urogenital apparatus (ureter, bladder, see lit., or prostate). The tubercle bacilli ascend in the stagnant urine to the kidney (ascending urogenital tuberculosis), and thus the disease is more often bilateral.

This theory has been disputed (Hochenegg, Garre-Borchard), but its possibility has been proved experimentally. (See Bauereisen, Sugimura, Ceelen.)

The tuberculous process then ascends from the pelvis to the surface of the papillae, and then to the angular edges of the calices, to the pyramids (Orth), to the border of medulla and cortex, etc.

Striae and nodules of caseous yellow masses are often surrounded by miliary tubercles containing quantities of active bacilli. Chains sometimes extend by way of the lymph channels to the outermost cortical layers. By confluence, larger caseous masses are formed which soften and produce cavities (Vomicae), their caseous peripheries broadening and destroying whole pyramids. Gradually, necrotic, glassy, gray, green, or brown fragments of papillae break off until cavities open broadly into the pelvis and extend to the cortex. Several cavities are often discrete, but in more advanced stages they all open into the pelvis as into a large central cavity. This is spoken of as the pyelitic form of renal tuberculosis.

Occasionally, we encounter a nodular form in which unilateral, or more rarely, bilateral, large, firm, conglomerate tubercles appear singly or in numbers. They infiltrate the parenchyma like a tumor and sometimes bulge on the surface as knobs or bosses with no tendency to softening.

Sometimes the infiltrations resemble large anemic infarcts of both medulla and cortex, without much change in the general shape of the organs; this is probably tuberculosis of vessel walls, (p. 131). The capsule may be perfectly intact, or a fungoid perinephritis may be present. When the pelvis remains free of the disease, it is spoken of as closed renal tuberculosis, but if there is only slight ulceration, of a single papilla, for instance, the pelvis will show disseminated tubercles or lenticular ulcers.

If there are no other tuberculous foci in the body we may call it primary renal tuberculosis; it is assuredly very rare on the autopsy table, for we usually find pulmonary or intestinal tuberculosis, or at least a caseous or chalky bronchial or abdominal lymph node as proof of former infection.

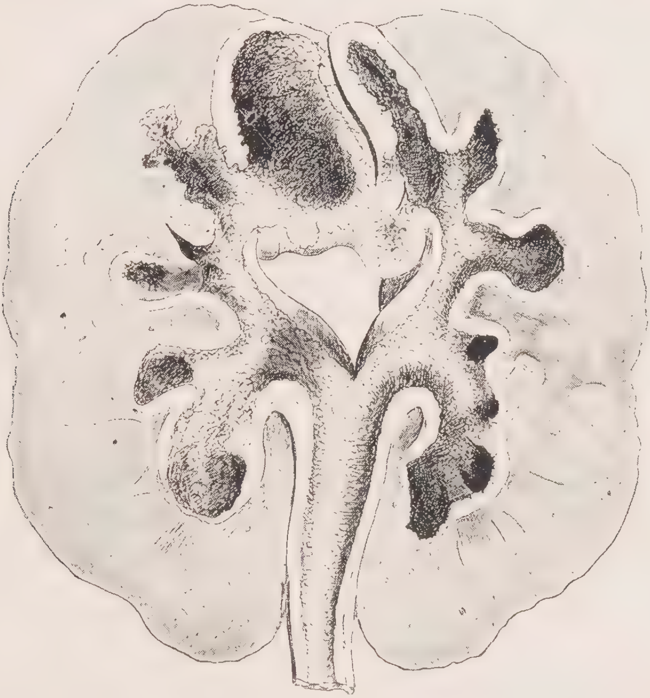


FIG. 711.—Tuberculosis of kidney; caseous tuberculosis of thickened ureter, pelvis and calices. Above, an especially large cavity extending from below capsule to the pelvis. Longitudinal section through kidney, presenting each half separated; ⅔ nat. size.

In unilateral renal tuberculosis (tuberculous surgical kidney with pain in bladder and kidney), Tendeloo thinks of lymphogenous infection retrograde from para-aortic lymph nodules rather than hematogenous infection. This opinion is not shared by Wegelin-Wildbolz, but lymphatic communications between the two kidneys makes possible infection of one kidney from the other. Besides this, we see extension through the urinary channels (via bladder), from one kidney to the other.

Caseous cavernous renal tuberculosis may be uni- or bilateral; in the latter it is usually not equal in severity. The size of the kidney varies considerably; it may be smaller, but sometimes is enlarged to more than twice its normal size. It can be of fluctuating consistency and may show on its surface fluctuating, white, rounded bosses, between which are scarred depressions. The capsule is often thickened and brawny, but the kidney is often quite easily shelled out. In time, the entire parenchyma is destroyed, and if the ureter is occluded by caseous masses or tuberculous infiltration of its walls, the kidney becomes a sac with thickened connective tissue walls containing caseous, purulent, or turbid white, cheesy masses, soft and sour smelling. Partitions may divide the sac into more or less numerous compartments (caseous pyonephrosis). If but one kidney is involved and shrunken, (see below), the other kidney exhibits compensatory hypertrophy.

The author saw a case, (31 year old male), in which one tuberculous kidney weighed 30 gms., while the other, also caseous and cavernous, weighed 345 gms. In another case, (68 year old man), the left tuberculous kidney weighed 30 gms., while the healthy right kidney weighed 206 gms. In still another case, the right kidney had been operatively removed some time before and the left caseous kidney weighed 700 gms.

(The normal weight of both kidneys is 250–300 gms., in women about 25 gms. less. The left kidney is usually heavier and larger than the right.)

The quantity of urine is normal if the other kidney is healthy.

The author saw a 19 year old laborer from whom it was necessary to remove an accidentally crushed, healthy right kidney, markedly hypertrophied. Twenty days later the patient died of uremia. The left kidney weighing 450 gms., had become a cavity system larger than a fist filled with desiccated cheesy material, while its ureter was completely obliterated.

A picture deviating from the typical caseous ulcerative form results if the ureter is obliterated. The debris desiccates and becomes partly fibrosed; the remnants of the parenchyma atrophy or undergo cicatrization, (see Harbitz). Finally the kidney shrinks (to 30–15 gms.) and on cross section, rounded or angular masses, yellowish white, putty- or ointment-like, may be squeezed from the cavities; a remnant of the pelvis may be preserved.

On rare occasions, we find the contents a milky or watery fluid, while the walls of the cavities are fibrosed. This is a healing process, but it usually occurs only in isolated cavities. Sometimes the organ shrinks beyond recognition, and then the tuberculous process may be considered as finished—healed. (V. Harbitz.)

See Ceelen, and Schonberg in regard to tuberculous contracted kidney, due both to tuberculous processes in the arteries, leading to destruction of the parenchyma, and to interstitial tuberculous connective tissue proliferation. It is a part of the process of repair, and also of non-specific inflammatory reactions. Complete healing may take place in this way. (Harbitz.)

The pelvis is infected in the vicinity of one or another caseous pyramid, or in typical cases, as a whole. Distinct nodules, or ulcers, or cheesy granular, or cheesy villous masses coat the inner lining with a thick layer; externally, younger, glassy gray or gray red tuberculous granulations or cicatricial tissue are an accompaniment. The contents are whey-like, purulent fluid with an ammoniacal odor, or grumous, or creamy, or cheesy pus (caseous pyonephrosis). Sometimes the contents are tallowy or putty-like, or doughy. Incrustations of earthy phosphates, or free phosphatic calculi are not rare.

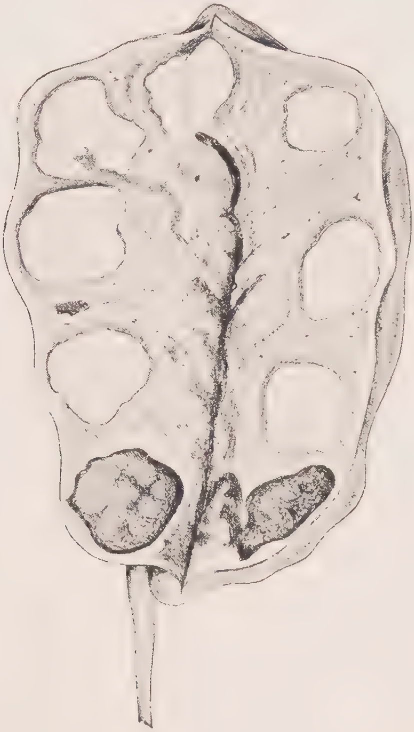


FIG. 712.—Atrophy of r. kidney by tuberculosis with obliteration of ureter. The unrecognizable parenchyma of the organ contains cavities filled with caseous purulent masses; below, remains of pelvis. The other kidney, the ureter as thick as the little finger, showed typical cavernous tuberculosis; weight 265 gms.; man 33 years old, with genito-urinary tuberculosis (bladder, urethra, prostate, both vasa deg., both epididymi, r. testicle and tuberculosis of lung); 9/10 nat. size.

Occasionally we find the pelvis and perhaps the ureter also, coated with shiny laminated layers like asbestos or fish scales, consisting of keratosed epithelium, fat droplets and cholesterin.

The ureter undergoes the same changes as the pelvis. It shows scattered ulcers or caseous infiltrations and becomes thick walled and firm.

As a rule, with the exception of the entrance into the bladder, it is dilated, occasionally as large as a thumb or more, due for the most part to the damming back of urine behind the entrance into the bladder. An ascending infection to the kidney is thus favored, and the vicious circle consists of the ureter infected by a descending tuberculosis carrying an ascending tuberculosis to the parts above, *i.e.*, the pelvis and the kidney. The ureter may be stenosed, even at several places, and become varicose and caseous, or caseous and fibrosed, or, as the author saw, obliterated throughout its length by cicatricial fibrous tissue.

In such closed tuberculous caseous pyonephroses, the urine contains no tubercle bacilli. Another cause of occlusion of the ureter is fragments of caseous material, in one case, (65 year old woman, old pulmonary phthisis, bilateral caseous cavernous renal tuberculosis), the author found the left ureter occluded for six cms. of its length by transparent grayish green fragments of necrotic papillae.

As already mentioned, the lower urinary tract is often infected and the urine contains, although in variable amounts, pus, debris, tubercle bacilli, and blood.

According to J. Israel, blood is present in the early stages, and even when the urine is clear, it can be found in 25% of the cases. The bacilli appear in the urine frequently, although not constantly, sometimes in such large numbers, that S-shaped, snake-like and caterpillar-like groups (braids) can be seen macroscopically on the stained slide. This particular arrangement is a point of differentiation between tubercle and smegma bacilli with which they are easily confused, especially in naturally voided urine of women. In catheterized urine, smegma bacilli are infrequent, (see under penis; lit. by Salus). See Bender for the staining of tubercle bacilli.

Consequences. While multiple disseminated miliary tubercles are of no great pathological importance and cannot be diagnosed clinically, the localized tuberculosis, much more frequent in men than women, is often a dangerous disease, especially in its typical caseous-cavernous form, not only because of its local destruction of kidney tissue, and the danger of interference with kidney function, but also on account of the danger of transmission of the tuberculous process to the lower parts, (descending urogenital tuberculosis). There is the possibility of an acute general miliary tuberculosis to consider, as the author observed in an 83 year old woman with left renal tuberculosis. In a case of Hanau, the general infection was transmitted through the tuberculous renal vein. In the closed form, caseous nodular perinephritis is comparatively frequent, but relatively rare in the open cavernous tuberculosis, (lit. in ref. to renal tuberculosis in appendix).

Syphilis of the Kidney.—(Lit. by Herxheimer, F XI, I part 1907, and by Brault and Courcoux.)

In the secondary stage of syphilis there often occur degenerative changes in the renal epithelium, accompanied by marked albuminuria and the excretion of lipoid substances, (Munk). This is designated by clinicians as a toxic nephrosis (Munk, lit.; see p. 1321) or as an epithelial nephropathy. Differentiation from mercury or salvarsan effects is difficult. It has occasionally proved fatal, and has been combined with grave hepatic degeneration (malignant degenerative syphilis), although most cases are favorably influenced by specific treatment (see Lichtwitz). Tumor-like gummatous nodules and cicatricial gummatous proliferations with scarred indentations are rare, but the former have caused marked enlargement of the kidney. (Roessle.) In the late stages a condition known as syphilitic contracted kidney may appear resembling the common contracted kidney, but the scars are confined to circumscribed areas on the surface showing mildly characteristic, gray, stellar or wedge-shaped atrophic foci, showing obliterating arteritis and hyalin glomeruli. It can be differentiated from focal simple arteriosclerotic atrophy by the more marked proliferation of granulation tissue in the periphery of the foci. It has also been called multiple fibrous interstitial nephritis, and according to Munk, may be the finale of a toxic nephrosis. (See above.)

Amyloidosis also occurs, but the most frequent clinical syphilis is arteriosclerotic contracted kidney without specific character. (See Munk, lit.)

In congenital syphilis, the kidney is often changed. As emphasized by Hecker, among others, the kidney, in contradistinction to the liver, may still be examined in the decaying fetus. There are not merely diffuse or focal small cell infiltrations but also increases of the interstitial connective tissue with vascular and perivascular infiltrations, chiefly in the cortex but also in the medulla. In the syphilitic newborn and suckling, focal and diffuse fibrosis may be found (rarely) in conjunction with vasculitis and fatty degeneration of the parenchyma, (diagnosis must be carefully weighed, see p. 463). Induration contraction is rare. Compression of the uriniferous tubules in the medulla followed by cyst formation has been observed. (Stroebe.) Larger gummatous nodules are seldom found. Ribbert, Perrando, described peculiar large cells resembling protozoa. Care is necessary in diagnosing cellular infiltrations because they are normally present in the fetal cortex although less abundant and with larger cells poorer in chromatin. (Ruckert.) In reference to the assumption of growth inhibition by syphilis (Stroebe, Hochsinger, Stoerk), as far as it concerns the appearance of the convoluted tubules in the cortex ("neogenetic" cortical zone, Hamburger), it may be pointed out that the same picture is found in the healthy fetus, and even in normal infants carried to full term. (Hecker.) According to Ruckert, isolated, poorly developed glomeruli are found in the normal kidneys of the newborn and they probably become the calcium bodies of the cortex described by Baum. (See p. 1331.) But Kimla (lit.) has shown that there is actual inhibition of parenchymatous development along with proliferation of the mesenchyme, which in its structure (cellular elements), remains in a state of development not corresponding to the age and development of the individual in question. Hecker (lit.) considers the cellular infiltration of the walls and vicinity of the smaller cortical arteries most important and pathognomonic of syphilis. Ceelen mentions plasma cells as a typical finding because they are absent in healthy fetal kidneys. Block (lit.) reported hematopoietic foci (chiefly erythropoietic) in a syphilitic baby of 6 weeks. (For polycystic kidneys, see p. 1385.)

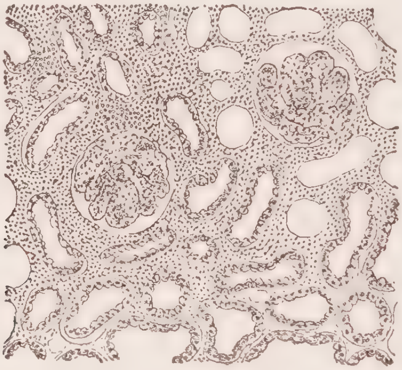


Fig. 713.—Diffuse lymphocytic infiltration of interstitial tissue of kidney of leucemia. In some tubules the epithelium has fallen out (artefact).

Actinomycosis of the Kidney.—Renal foci appearing by contiguity or metastasis from infection of other organs are very rare. They may reach considerable size. Actinomycotic perinephritis has been reported. (See Th. Cohn as to actinomycotic pyelonephritis; see Kunith, J. Israel as to supposed primary actinomycosis; also lit. by Brault and Courcoux.) Picture of an actinomycotis abscess by Ponfick.

Lymphoma-like cell masses in the kidneys occur in a number of infections, such as typhoid fever, small pox, scarlet fever, etc. In leucemia, aleucemia, and rarely in lymphosarcoma (see Fabian lit.), the cell collections may be diffuse, and so massive that the paired organs become much enlarged, spotted gray yellow and glassy in appearance where the architecture is obliterated; or circumscribed tumor-like nodules appear. (See the author's observations pages 276–279, 1395.)

Hematogenous Deposits in the Kidneys and Pelves

The kidneys, acting as the chief purifying apparatus of the blood, are often the seat of deposition of substances which are either present as solid bodies in the blood stream, or more frequently as dissolved substances precipitated after reaching the kidneys. These substances are in part normal excretory products which for some reason are precipitated, *e.g.*, the uric deposits in dead epithelium; others have nothing to do with normal secretion.

(See lit. by Brugnatelli *in re* experimental work dealing with the absorption and elimination of coloring matter by the kidneys.)

Solid excretions (not only of urinary salts) in the kidneys themselves have been called from early times by the poorly chosen name of "infarcts."

Uric Acid Infarcts and Gouty Foci.—The uric acid infarcts of the newborn are yellow or brick red, striped masses in the papillae extending more or less into the medullary substance and converging in fringes to the apices. The light fan-shaped stripes contrast sharply with the dark red color of the medullary substance. They are uric acid, *i.e.*, uric acid salt, deposits in the collecting tubules and the papillary ducts.

When squeezed from the papillae and placed under a microscope they appear as dark, friable cylinders and sausage-shaped structures ranging from light yellow to brown or even black; some are radially striated and of double contour, (so-called spheroliths, doubly refracting in polarized light) consisting of ammonium urates and, rarely, sodium biurates. When dissolved in hydrochloric or acetic acids, flat uric acid crystals precipitate on evaporation, some in typical whetstone form. A clear light clot of albumen remains, the organic scaffolding (Ebstein), which, like the uric acid globules, is eliminated by the epithelium of the convoluted tubules. (Eckert, lit.) Hyalin casts may also serve as scaffolding to uric acid casts and these may be recognized as such even after solution of the urates by formol hardening. Some of the uric acid salts are excreted in solution. (See Aschoff.)

This excretion is physiological and interpreted as an expression of uric acid excess in the blood (Virchow), resulting from the metabolic changes starting after birth. M. B. Schmidt (lit.) believes that the active destruction of leucocytes after birth is the chief factor in causing this excess. The uric acid infarct appears only, although not without exceptions, in such infants who have lived and breathed. (v. Hofmann.) Elimination practically never begins during the first day, but takes place usually from the second to the fourteenth or twenty-first days. As a rule the "infarcts" are washed out by the urine without difficulty, but, they occasionally remain longer in the kidney, the pelvis or the bladder as yellow brown granules or are found later as concretions the size of a lentil. Orth mentions such findings in a 5 year old boy, and the author saw them in a 7 year old boy who died of rabies. The urates may be washed into the pelvis or the bladder and lead to the formation of larger calculi composed mostly of acid ammonium urates, a frequent calculus, especially of children. Perhaps the infarct is, so to speak, the acute state of uric acid calculi. (M. B. Schmidt.) Bilirubin infarcts are often combined with the uric acid types (p. 1377).

In leucemia, uric acid is frequently increased in the urine and the infarcts are common, but in this case cellular disintegration is probably the deciding factor. M. B. Schmidt saw occasional infarcts with sarcoma, but never in carcinoma.

In adults with arthritis urica (gout), intensely white stripes or spots, mostly in the medulla, but also in the cortex, are crystalline heaps of sodium bi-urate and acid ammonium urates. They are the so-called gouty tophi to which lime is added which alone is not so intensely white. A contracted kidney is often present, but apart from the tophi, many kidneys are otherwise unchanged. The contracted kidney is found chiefly in older cases of gout complicated by tophi (see p. 1253), and opinions are still divided as to its origin. According to Ebstein, it is primary to a gouty predisposition, (primary renal gout in contradistinction to articular gout), or is secondary to injury by uric acid salts. Brucksch and Schittenhelm believe in the existence of a "metabolic gout" and a "renal gout" as main types of the disease; thus in gout of the kidneys, the metabolic changes follow simple contracted kidney because the latter causes retention uricemia. But there is no lack of objection to this conception, since contracted kidneys generally do not cause urate deposits. (See Tollens.) The question requires further elucidation.

Microscopically, the tophi differ entirely from uric acid infarcts. Thin long needles and larger crystals (rhombic pillars and plates) are gathered in fan-shaped bundles in the uriniferous tubules, especially in the medulla, but also sometimes in the epithelium, and (according to Ebstein, even exclusively) in the interstitial parts. The tissue surrounding them is necrotic and nuclear staining is impossible. This, according to Ebstein, is due to the effect of dissolved uric acid; deposition of crystals takes place after the necrosis, (for other opinions, see p. 1252). The crystalline deposits are then often surrounded by spindle and epithelioid cells and sometimes by many foreign body giant cells (p. 1253).

The plates and pillars (needles) of uric acid salts dissolve in warm hydrochloric or acetic acids; after cooling, whetstone-shaped crystals are deposited.

Larger uric acid concretions (gravel and calculi) which sojourn in the tubules and especially in the pelvis, and which appear frequently in gout, will again be mentioned under "nephrolithiasis," (p. 1409).

Blood Pigment Infarcts.—Hemoglobin (see hemoglobinemia p. 186), or methemoglobin infarcts (as in poisoning by chlorides, see p. 215) are often produced when there is destruction of erythrocytes within the circulating blood. The pigment is found in the form of red, yellow or brown droplets or finely grained brown masses molded into casts in the lumena of the uriniferous tubules; the latter also contain hyalin casts. In severe cases the kidney is enlarged, light brown, and the pyramids are clearly striped and spotted.

The epithelium of the convoluted tubules may be diffusely saturated with hemoglobin so that within the tubules granular hemosiderin is found. According to Miller, the hemoglobin is excreted by the convoluted tubules and Henle's loop. The urine is red to brown in color, and at times almost black.

Deposits of hemosiderin (iron-containing moiety of hemoglobin), often occur in hemosiderosis, and extensively in pernicious anemia. For conditions in malaria see p. 208. Deposition is in the form of clumps and granules chiefly within the epithelium of the convoluted tubules (according to Paszkiewicz exclusively in the cortex), in the capsular epithelium and in the endothelium of the capillaries. Pigment is also found in the lumena of the tubules and vessels. Many cells show diffuse infiltration.

Deposition of hematoidin (iron-free moiety of hemoglobin) occurs in the form of granules and crystals, (iron reaction p. 372).

The fat-containing physiological pigment lipofuscin (p. 1311) must not be mistaken for hematogenous pigment.

Bile Pigment Infarcts.—In the icteric newborn, the bilirubin infarct is to be found (E. Newmann), usually combined with uric acid infarcts. Macroscopically, it is an orange red radiating mass in the papillae from which a putty-like substance may be squeezed.

Microscopically, bilirubin is partly amorphous, light yellow and granular, and partly crystalline in bundles of ruby red needles or rhombic structures. The masses lie in the medulla, in the lumena of the tubules, in the epithelium, blood vessels, and interstitial tissue. They are less frequent in the cortex. They are also in the blood, in the various organs, and particularly in fatty tissue.

In the icterus of adults, bile pigment is precipitated and stains the kidney grass green by bilirubin, or biliverdin, if the icterus is of longer duration. The precipitate as a rule is not crystalline.

According to Orth, crystalline bile pigment is deposited exceptionally in acute atrophy of the liver and in pernicious anemia with icterus, but the precipitation is probably post-mortem. The epithelium in the medulla, but more in the cortex, is stained diffuse yellow and green; the pigment is often clumped to granules which fill the tubules both convoluted and straight, with masses or compressed casts. The more heavily pigmented epithelium, especially that of the convoluted tubules, undergoes fatty degeneration, or necrosis and exfoliation, an injury caused by the bile acids. Bile stained hyalin casts as such, or covered with pigmented cells, are numerous. The medulla may show dark green stripes. (See Ulrich in reference to other renal excretion-pigmentation.)

Calcium Infarcts and Other Calcifications.— Calcium infarcts are composed of calcium phosphates and carbonates in white striae radiating upward from the apices of the papillae. The most frequent form is the senile type, found in advanced age. Other conditions, *e.g.*, osteomalacia and fibrous ostitis, in which there are active absorption processes in the skeleton, are accompanied by lime deposition in the medulla and cortex as so-called lime metastases.

Microscopically, the lime infarct of advanced age, consists, as M. B. Schmidt has emphasized, (see also Goldschmidt), chiefly of a finely granular deposit in the interstitial tissue and the tunica propria after previous hyalin degeneration. Hyalin casts frequently calcify in the medulla and assume nodular shapes appearing black by transillumination and shining white with reflected light. (For calcium reactions see p. 102.)

According to Kuhn (Lubarsch), various conditions which cause local changes in the papillae are responsible for this deposit; they are grouped as inflammatory, simple circulatory, nutritional, and senile disturbances. Goldschmidt demonstrated its frequent association with cirrhosis of the liver, explained by an increased content of calcium in the tissue fluids meeting local renal conditions. (Kuhn.) It is confined to the pyramids.

In calcium metastasis, the increased calcium content of the blood is responsible, first, for the lime incrustation of the stroma and the vessel walls, even of the glomerular loops and capsules, and for precipitation in the epithelium, and secondly, for calcium cast formation in the lumena of the tubules. This change involves medulla and cortex. Larger concretions are frequently found in the pelvis. (See Wells for generalities as to metastatic lime deposits.) Such cases are designated as calcium gout (M. B. Schmidt) in which the internal organs are favored first in calcium metastasis (lungs, stomach, kidneys) and show a typical picture with absent skeletal changes. On the other hand, there is a type of nephritis which is considered the favoring factor in the precipitation of calcium salts. M. B. Schmidt thinks that a decrease of albumen in the blood from increased elimination changes the solubility conditions in reference to calcium, permitting precipitation of some of this substance in those organs predisposed to it.

He furthermore points out that in carcinoma, even if there is no bone destruction, there are, without exception, chalk casts in the straight tubules of the medulla.

In various poisonings, although not constantly, there are often found macroscopic, at other times only microscopic, extensive spotted deposits of lime salts in the necrotic epithelium, especially in the convoluted tubules. Such a poison is corrosive sublimate.

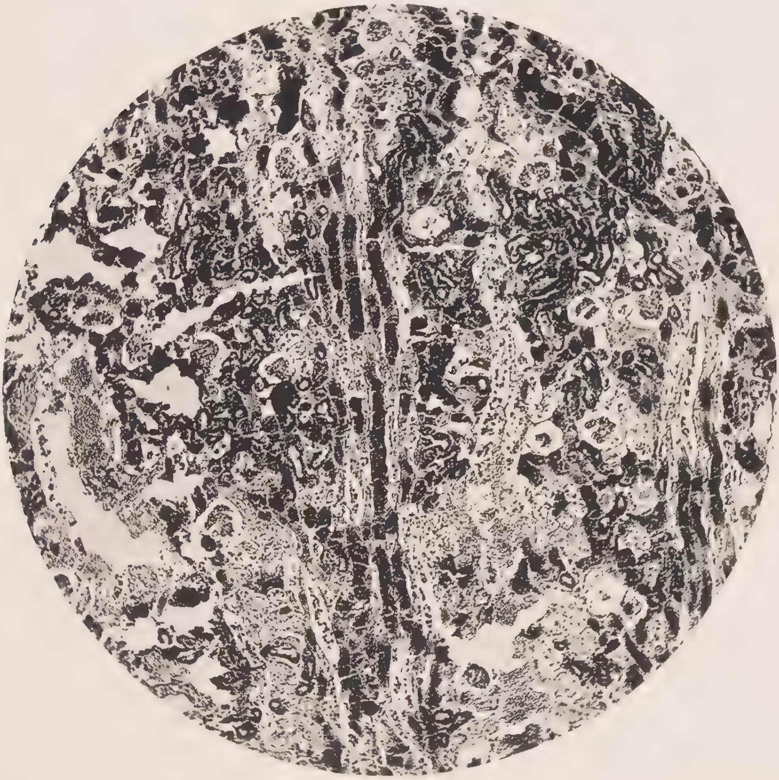


FIG. 714.—Rabbit's kidney showing the development of so-called calcium infarcts after mercury poisoning. This rabbit was given repeated doses of novasurol, an organic mercuric preparation, was killed on the tenth day and both kidneys were found in the condition as represented in the print. Further experience showed that calcium is deposited in this poisoning as early as the third day. × 120. L. H. #1083.

It has been observed, but inconsistently, in experimental poisoning with glycerine (Afanasjew), phosphorus, aloin, bismuth subnitrite (Newberger), naphthol. In the rabbit, the physiological calcium content of the blood is high, and possibly this is the reason that the epithelium calcifies as soon as toxic necrosis is begun. It is seen in iodoform and formalin poisoning. In poisoning with amanita in man (p. 910) calcium casts are found, and are interpreted by M. B. Schmidt as precipitations within the lumen and not as incrustations of dead epithelium.

In the calcification of mercury poisoning, only the necrotic epithelium is involved, especially of the convoluted tubules and the ascending limbs of Henle's loops (differences of opinion between Suzuki and Weiler). (For calcium reactions see p. 102.) This opinion emphasized by the author in opposition to Virchow's statement that the lime in calcium metastases fills the lumena of the tubules, was verified by Heineke and others in opposition to Leutert. Heineke pointed out that a simultaneous (earliest on the 3rd day) active proliferation of the surviving intact epithelium takes place coupled with phagocytic activity toward dead cells and lime granules; giant cell formation also occurs. These are regenerative and healing processes but do not always prevent death, which usually occurs within the first eight days, while in the subacute form of mercury poisoning they may be of greater importance (comp. Toppick). Detached calcified epithelium forms chalky casts which also contain iron. (Gierke.) The glomeruli are not involved, and it is probable that occlusion of the uriniferous tubules with necrotic cellular debris prevents the outflow of urine and is thus responsible for the anuria. M. B. Schmidt thinks that calcification of dead epithelium is due to insufficiency of the mucosa of the colon which normally eliminates 90–95% of the calcium. Only a combination of renal and colonic injury makes possible the calcification. (See also the observation of M. B. Schmidt in severe dysentery, naphthol poisoning of renal epithelium, and renal calcification.) In early mercury poisoning, necrosis of only the tubular epithelium is found, probably not a direct effect of the eliminated poison, (see author), but a consequence of obstruction to vessels, (see Weiler, lit., Ricker, Strache, and others, lit. p. 770). The cortex is cloudy and pale and the process may be mistaken macroscopically for fatty degeneration, which may, however, be present, (without protagon—Stoerk; p. 1320). Constantini verified these findings in experimental sublimate poisoning. Askanazy and Nakata, in 15 cases, could distinguish three stages of sublimate nephritis: (1), the red initial stage, (2), the grayish white kidney usually found from the second day to the end of the first week, (3), the red sublimate kidney in a narrower sense, to the 17th and 18th days. At this stage, the diffuse calcification is found. In rabbits which have a high calcium content in blood and urine, calcification begins in one day, but in dogs with their low physiological calcium content, it often remains absent. Castaigne and Rathery describe the minute changes, especially of the granules, (see also Munk as to sublimate nephrosis). Faccine also saw in sublimate poisoning, such degenerative changes in the sweat glands as detachment of epithelium, poor staining, fatty degeneration, etc., which he considers dependent on the renal changes.

In phosphorus poisoning, there is the typical marked fatty degeneration, first of the epithelium of the convoluted tubules, but finally of that of the other tubules also. (Experimental, see Herzog; comp. Lohlein.)

In poisoning with oxalic acid and potassium oxalate, calcium oxalate is precipitated in large quantities in the kidneys and the pelves in a very short time (15 min. or less), if the quantity of sodium phosphate is insufficient to hold the oxalic acid in solution. The oxalate forms white precipitates lying within the convoluted and straight tubules, but Kruger saw crystals in the epithelium also. The tissue elements, however, are not demonstrably injured. Oxalate calculi in the pelvis are brownish yellow or brownish gray. In reference to bran-like white excretions on the intestinal and gastric mucosa, see p. 676.

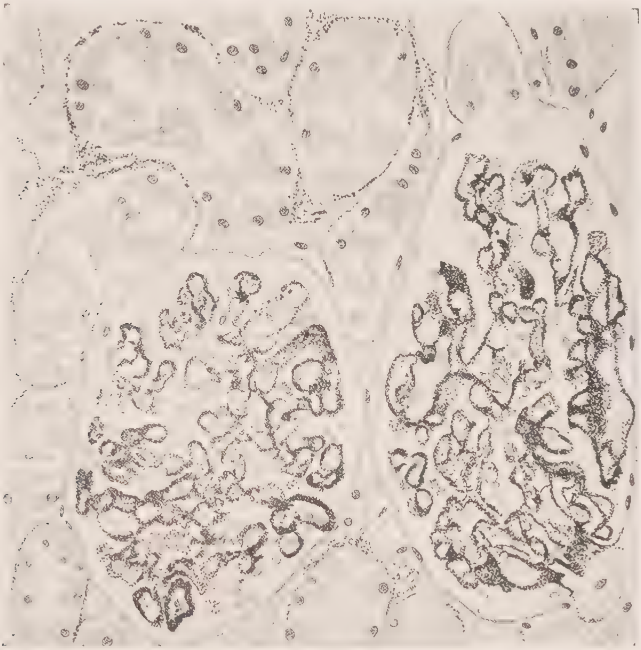


FIG. 715.—Argyria of kidney (so-called silver infarct). Deposit of silver salts as fine granules in the walls of the glomeruli, in the tunicae propriae and in the interstitial tissue. Epithelium is much detached, partly post-mortem, partly artefact. (High power.)

Fat Infarcts.—This is a fat deposit, usually in the form of minute droplets in the interstitial tissue, easily demonstrated by staining. They are found around vessels and uriniferous tubules in the vicinity of the renal papillae, but the tunica propria of the straight tubules may also be involved. Fat and calcium infarcts are occasionally combined, (see Prym, Kaiser, Petersen, Kuhn).

So-called Silver Infarcts. This rare infarct occurs in argyria which sometimes develops after the continued use of silver preparations. Tiny brownish black silver granules are deposited in large numbers within the walls of the loops of the glomeruli, and in the connective tissue, especially in the tunica propria of the medulla, which may appear gray to black, (lit. by Dohi); (see also under skin). See Fahr (lit.) as to possible injury to the renal parenchyma by absorption of collargol with which the pelvis is filled during pyelography for diagnostic purposes.

Cysts, Tumors, and Animal Parasites of the Kidneys

Cysts.—**Isolated cysts** are occasionally seen in otherwise healthy kidneys, especially in older people; they are rarely larger than a cherry to a walnut, but sometimes a single cyst is as large as a man's head, with the inner surface lined with pavement epithelium.

In the watery clear content of these large cysts no urinary substances can ordinarily be traced, except albumen. Sometimes the content of smaller cysts is colloidal and brown. Their origin is probably a fetal developmental inhibition combined with secondary snaring off processes. (Ruckert.) Braunwarth (lit.), too, considers them congenital, and only quantitatively different from the true cystic kidney, (see below; see also Coenen).

In reference to the surgical treatment of these large solitary renal cysts, see Brandenstein (lit.), Sonntag (lit.). For solitary hemorrhagic cysts, see Wulff. [For calcified renal cyst, see Kirwin, T. J., J. Urol. 15: 273: 1926.—*Translator*.]

Multiple cysts are usually small, from the size of a millet seed to a pea; they are frequent in the contracted kidney, especially in its true form, but also in arteriosclerotic and senile atrophy. Sometimes they cover the whole surface of both kidneys, but the organs are not necessarily enlarged thereby.

The contents are at times clear fluid like urine, at other times, colloidal. They are either retention cysts, *i.e.*, urinary retention on account of occlusion of occasional or many tubules, or secretory from pathological cells as in colloid cysts.

The author saw numerous small cysts, with numerous peculiar whitish yellow tumors in the kidneys (Fig. 721), in tuberous cerebral sclerosis.

Cystic kidney, or so-called cystic degeneration, or renal cystic hydrops, is met in adults, even in advanced age, and in the newborn and children, as the congenital cystic kidney.

The process is usually bilateral; the cysts are very numerous and form a system of rounded cavities of various sizes, separated by septa often showing traces of renal parenchyma. The separate cysts vary in size from a pea or a cherry to larger than a fist. The clear contents usually shine through the bluish white or golden yellow cyst walls. They are chiefly in the cortex, but also at times in the medulla in which they are seldom very numerous. The contents are serous with abundant albumen; isolated cysts may contain yellowish colloidal substances red or brown, clear or cloudy from hemorrhage. The author saw a case of septic pyemia (41 year old man with slight lesion on big toe) in which some of the cysts contained purulent fluid, (lit. regarding infected cystic kidney by Sieber, Bull). The cysts bulge more or less on the distorted surface. In extreme degrees, the kidney resembles a bunch of grapes of varying sizes; the organ as a whole is frequently as large as a child's head or more, and weights of 3000 gms. have been recorded. The author saw two kidneys weighing 3054 gms., one of which was 28 cm. in length. Cystic kidneys usually sink downward as far as the linea innominata or lower. Frequently a cystic liver is coincident. Specimens with chief localization of the cysts in the medulla (medullary cystic kidneys) are quite rare in comparison to the diffuse varieties. There are transitions, of course, with numerous medullary cysts to those with but occasional ones. (Stammen, lit.)

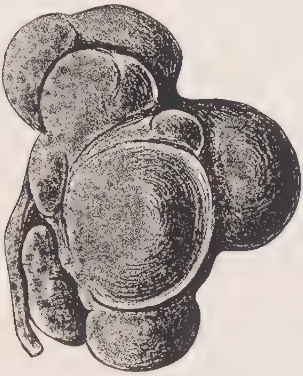


FIG. 716.—Cystic right kidney of a stillborn female child with congenital syphilis; weight 24 gms.; nat. size.

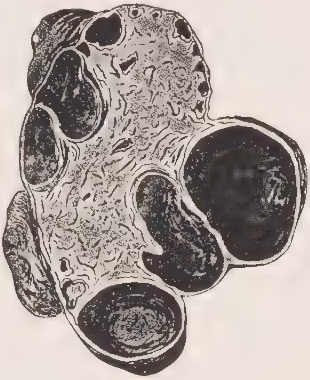


FIG. 717.—Frontal section through this kidney. The other kidney was not cystic.

Individuals with cystic kidneys often reach advanced age, but sometimes they die quickly of uremia. According to Kummel, hemorrhage is one of the chief clinical symptoms, but the author has never observed it in any of his cases.

Ruckert points out that malformations and developmental disturbances, especially in other parts of the urogenital system, are often found in conjunction with this type. Dunger (lit.), Bull, and others call attention to a familial and hereditary predisposition, (see also Jungmann). Partial cystic kidney is very rare. (R. Meyer, Jaeggy.) Cystic kidneys in the newborn are usually bilateral and sometimes show no, or only slight enlargement, (small congenital polycystic kidney); they may even be too small, (hypoplastic cystic kidney; see Mount); they then resemble a finely porous sponge or a compact mass of sago, or a mulberry with innumerable small cavities. (Lit. by Staemmler.) In other cases the cysts are much larger and usually less in number as in the large congenital polycystic kidney, the weight of which may be increased a hundred fold and actually be an obstruction to childbirth. (Lit. Hennig.) As stated, the liver may also be polycystic; the author saw the pancreas in a similar condition, but this is rare. In the congenital type, the papillary and adenoma-

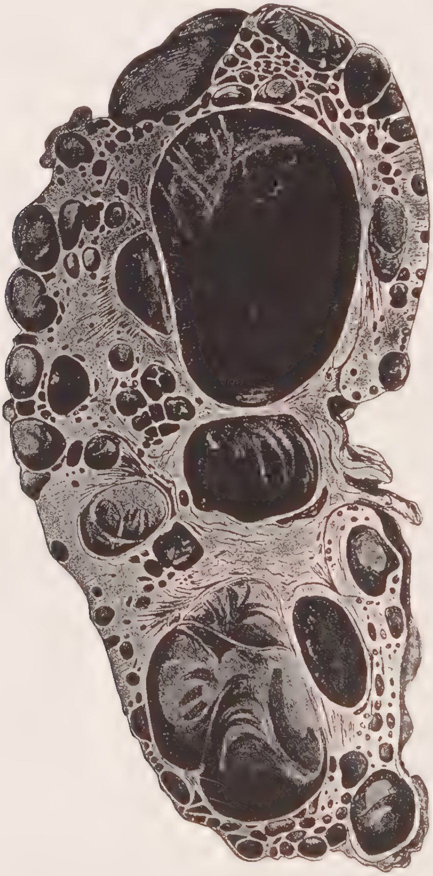


Fig. 718.—Cross cut through a cystic kidney of a woman 50 years old; other kidney similar. There was also a cystic liver. Sectioned after hardening in formalin. The contents gelatinous, coagulated, were removed; ⅔ nat. size.

like proliferations, so frequent in the cystic kidneys of adults, are generally absent. (Dettmer, Ruckert, Erich Meyer.)

Many different opinions are expressed concerning the cause of cystic kidney, but it is probable that it is always congenital and due chiefly to developmental disturbances. Thus far no satisfactory solution which covers all points has been offered.

Older opinions laid much stress on retention, due to obstruction of the tubules from inflammation. For instance, Virchow believed atresia of the papillae, perhaps due to small uric acid concretions in the tubules, was responsible. Thorn accused a papillary nephritis extending from the pelvis, but this idea was found untrue not only by general experience but also by special experiments in which ligation of a tubule caused atrophy. (Tollens, Petterson.) Others assume that there is proliferation between the renculi, (Durlach), or consider the straight arterioles the point of attack of an "inflammatory stimulus" (Leichtenstern). Arnold thought there was a primary "fibrous nephritis" as did the author in the case last mentioned. Shukowsky and Ssinjoff emphasize the part played by chronic interstitial syphilis and consider the probability of its influence in the development of polycystic degeneration of the kidneys in childhood, (comp. the author's observation in fig. 716). On the other hand, almost all observers now believe that it is due to a malformation in the majority of cases, *i.e.*, to a developmental check, such as failure of certain urinary tubules to become patulous, and thus to connect with their ramifications (p. 1292), or secondary snaring off, followed by cystic ectasy of tubules and glomeruli from retention of secretion; to this, a secondary epithelial proliferation may be added or not, since it is not essential in the formation of a cystic kidney. The author is of the opinion that in the majority of cases this view is correct. On the basis of one case with hydronephrosis, Ribbert supports the theory advanced by O. Hildebrand, viz., that they are retention cysts depending on an inflammatory connective tissue proliferation induced by the hydronephrosis; the connective tissue prevents normal junction between the glomeruli and the straight tubules, while the convoluted tubules are checked in their development, and thus the formation of cysts both in the glomeruli and at the ends of the straight tubules is permitted. But Ruckert, who investigated several cases, demonstrated that the convoluted tubules were present. Erich Meyer, like Ribbert, speaks of an incomplete union of two systems. (See also Hornowski.) Ruckert, on the other hand, still holding to the viewpoint of the uniform development of the kidney (comp. p. 1292), assumes that the developmental inhibition is merely such that the kidney remains at an earlier or later fetal stage; the "snaring off" processes begin at predisposed places in the tubular system, especially at the physiological narrow places such as where a larger channel is formed by smaller tubules, *i.e.*, chiefly, although not exclusively, in the medullary papillae. The cause of this snaring off, which is analogous to that often seen in the ureters, is not settled, (epithelial adhesions, atrophy?). The earlier in fetal life this occurs, the more abundant is the connective tissue, especially in the medulla. This would explain the connective tissue increase (supposed inflammatory proliferation) described by the above mentioned authors.

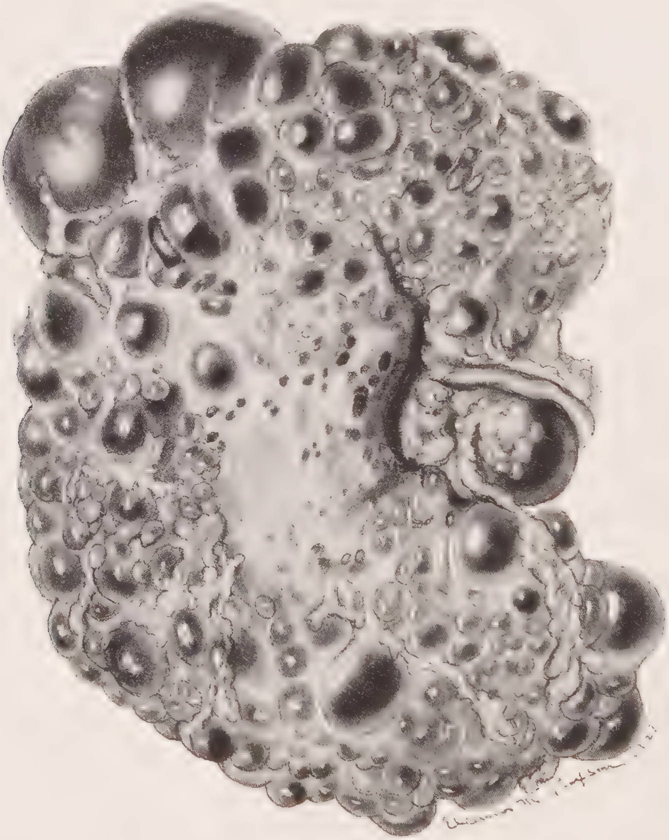


FIG. 719.—Congenital polycystic right kidney. Removal at operation because of the presence of a calculus and infection. In our experience most of these cases are bilateral. A most important point in the surgical thought is that even if only one kidney is polycystic at the time of operation and the other is normal to the palpating surgical hand, the second kidney is likely to become polycystic later when the one is removed. This has happened in three of our cases within the last three years. Possibly the increased demand for function with its resulting hypertrophy which takes place when one kidney is removed leads to the development of certain areas in the apparent sound kidney which later becomes polycystic. The average duration of life after the removal of one polycystic kidney in three of our cases was four years, the patients succumbing to uremia. There is a necessity for removal, however, not because it is polycystic but because of secondary complications such as calculus formation and infection. The areas in this particular kidney which show no cysts were composed of kidney parenchyma densely surrounded by old connective tissue. That there was some secretion from this kidney was proved by cystoscopic examination and ureteral catheterization but the largest amount of material collected from this kidney before operation was pus. L. H. #774. ½ nat size.

Borst, Dunger (lit.), and especially Busse, support the theory of developmental disturbance, but the first named believes there is a tendency in the epithelium to tumor-like proliferation and he speaks of neoplastic malformation, while the others consider the epithelial proliferation, which really does not occur in every case, as a secondary factor which may probably help the retention. (See also Albarran and Imbert, Zaccarini, Forssman.)

The cystic kidney of adults as well as the newborn has been considered an epithelial tumor, *i.e.*, as a multilocular adeno-cystoma derived from atypical glandular proliferation which develops in originally normal or abnormal kidneys. (Naunerck-Hufschmid, von Kahlden.) This opinion is difficult to prove, and is improbable for many reasons. (See Busse, Forssman.) The same idea is approached by the hypothesis of Birch-Hirschfeld, according to which the anlage of the uriniferous tubules of the normal kidney remain and give rise to a proliferation, or to true tumor formation. Brault and Courcoux consider the neoplastic theory the most plausible.

Berner (lit.) investigated twenty-eight cases, and while he assumes there is a constant developmental disturbance, nevertheless, he approaches the tumor theory by believing that a tumor-like proliferation, similar to Albrecht's hamartoma (p. 953), is frequently added, even approximating the appearance of a papilliferous cyst adenoma. He also observed cases in which islands of cartilage and horny pearls pointed to a true mixed tumor, (sclerodermic fragments). He found abundant smooth muscle, but never cross striated muscle in contradistinction to adeno-sarcomas. He likewise acknowledges the existence of rare cases in which all tumor indications are absent and in which true malformation is apparent. D'Agata, long ago, had stated that a cystic kidney is probably a true tumor perhaps connected with congenital malformation. Recently, Staemmler has expressed the opinion that it is a combination of congenital malformation and true primary tumor, a multilocular adeno-cystoma. (Lit. in appendix.)

Dyckerhoff thinks that certain unusual forms of bilateral cystic kidneys are due partly to lymphangiectasias or to cavernous lymphangiomata.

Renal Tumors

Epithelial Tumors. Adenomas.—These benign tumors are most frequent in older individuals, are usually in the cortex as rounded, sometimes porous, white, yellow (fat droplets within the cells), or brown (pigment from hemorrhages) growths. They are solitary, but sometimes multiple, and vary in size from a millet-seed to a walnut; larger tumors (to the size of a fist) are very rare. They generally spring from the epithelium of the cortical tubules. Developmental disturbances perhaps play some rôle.

According to Tilp, they arise in part from regenerative processes, just as believed for a long time in reference to the small multiple adenomas in contracted kidneys. (Comp. Silberberg.)

Simple and papillary adenomas may be differentiated, but there are transitions from one to the other. Simple adenomas are composed of irregular tubular cavities with high or low or cuboid epithelial cells contrasting with the highly organized secreting cells of the renal parenchyma.

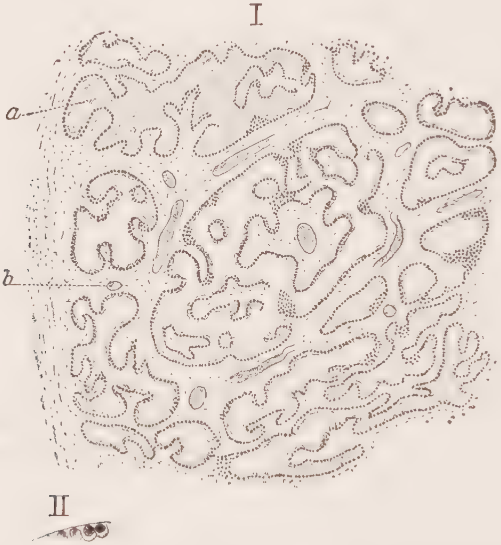


Fig. 720.—Papillary adenoma of kidney; tumor in cortex as large as a pea; a, gland tubules with papillary excrescenses, blood in tubules; b, blood vessels in stroma. (Low power.) II. Cell-lining of tubes. (High power.)

Papillary adenomas consist of delicate vascular papillary elevations in the walls of the tubules, proliferating into the lumena and often appearing, in microscopic preparations, free within the lumena. The cells of all adenomas often contain fat droplets. Hemorrhages into the lumena are frequent. The stroma is sometimes delicate, sometimes firm. There may be a definite fibrous boundary, or a kind of capsule which passes insensibly into the tumor and into the surrounding renal tissue. Sometimes large tumors of this type have the capillaries of the stroma surrounded by collars of high cylindrical cells reminding us of peritheliomas. Cysts and papillary adenomas are frequently combined, a fact used to support the conception that both depend on a malformation of the nephrogenous tissue. (Comp. Herxheimer, lit.)

Carcinoma.—The origin of primary carcinoma of the kidney is said to be both in the epithelium of the uriniferous tubules (Waldeyer, Beneke) and of the Malpighian bodies, (Roccavilla), although Ribbert considers the latter starting point highly problematical. The cells usually become atypical quite early and remind us very little of the original epithelium. Carcinomas may also arise from adenomas.

Hypernephromas, (p. 1395), are frequently classed with the carcinomas. These tumors are understood by Albarran and Impert to be cancers: (*a*) with clear cells, in contrast to the carcinomas derived from renal epithelium, and (*b*) with dark granular cells. Roccavilla believes he found transitions from (*a*) to (*b*) and quotes this finding as a conclusive factor against the hypernephromatous origin of the so-called hypernephromas of the kidney. Brault and Courcoux also speak of adeno-carcinomas with light or with dark cells, as well as of papillary carcinomas. They consider the question of Grawitz's tumors still in need of revision.

Renal carcinomas occur in children. The author saw a multilobulated white medullary adeno-carcinoma larger than a fist in a 12 year old girl.

In older individuals, renal calculi are occasionally found coincidently. Cancer is almost always unilateral, soft or firm, diffuse or nodular. The soft forms tend to diffuse distribution, sometimes involving the whole organ; they are white and often of extraordinary size, even to that of a man's head. The author saw one, 2720 gms. in weight, forcing the renal parenchyma aside or infiltrating it. From regressive changes, such as fatty degeneration, hemorrhages, calcification, necrosis, mucoid softening and cyst formation, the section surface is variegated and the differentiation from sarcoma may be quite difficult.

Nodular carcinoma is an irregular tumor in the cortex or a nodular aggregation forcing the parenchyma aside. These are often perfect adeno-carcinomas, but rarely papilliferous. (See Wohl.)

Cornifying pavement epithelium—carcinoma of the pelvis—may invade the kidney and reach its greatest development there, occasionally quite diffusely, (Milne). Scheel (lit.) described a cornifying carcinoma of the kidney combined with a papilloma of the pelvis showing cylindrical epithelium.

(Consult the section on "general behaviour of malignant renal tumors" p. 1400.)

Secondary carcinomatous nodules, usually rounded, appear chiefly as multiple growths in the cortex and, as a rule, are of hematogenous origin; histologically they are similar, generally speaking, to the primary tumor. The author saw pure sarcoma metastases in the kidney from a carcino-sarcoma of the thyroid. The metastases of malignant teratomas are frequently only carcinomatous. In a 25 year old female, the author saw numerous tumor emboli from a heterotopic chorio-epithelioma in the arterial branches of the kidney followed by anemic infarction. Lauterberg (lit.) described the invasion of carcinoma cells into the uriniferous tubules and Bowman's capsules. This may occur in primary renal carcinoma, as the author observed in a 72 year old man with squamous cell carcinoma of the pelvis.

Invasion of the kidney by the retrograde lymph route is rare, but the author saw such a case in a 54 year old woman with gastric carcinoma and peritoneal carcinomatosis. The growth did not form nodules, but a coating, with finger-like projections extending along the veins of the left kidney, especially along the arched veins at the junction of cortex and medulla. A secondary thrombosis had occurred in the trunk of the renal vein. (See the observations in similar cases by v. Recklinghausen, Vogel and Sinner.) (See Stahr, Kumita, for the renal lymph channels.)

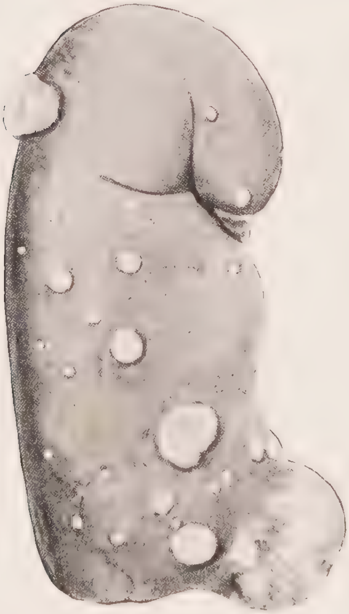


FIG. 721.—Multiple tumors of kidney (fibrolipomyomas) from a 10 year old idiotic girl with tuberous sclerosis of brain; other kidney similar; ⅞ nat. size.

Connective Tissue Tumors.—**Fibromas** are quite frequent; some occur as small nodules projecting somewhat above the surface, or as hemispherical or rounded masses in the cortex; or, more often as growths in the medulla near the base of the pyramids, (medullary fibromas). They often occur in both kidneys and are white, homogeneous, elastic, hard, and bulge on cross section. Uriniferous tubules may penetrate the edges here and there. According to Genewein (lit.) and Trappe, they are not true tumors, but tumor-like malformations, (fibrocanalicular renal hamartomas, E. Albrecht), an opinion now generally accepted, (see Hornowski). Large fibromas are rare; their origin is usually in the capsule. Thiede and R. Meyer saw an osteochondro-fibroma of the renal capsule.

Fibromyomas of the medulla are derived, according to Busse, from the smooth muscle fibres which are abundant in the medulla of the embryonic kidney. Hess described fibromyomas of the capsule; it must be remembered that strands of smooth muscle are normally present below this structure. Lartigau and Larkin saw multiple leiomyomas fused with the capsule, (origin capsule, or blood vessels). Hallas described a fibromyo-endothelioma.

Hemangiomas (rare) may cause hemorrhages if they are in communication with the pelvis. Fukuda described cavernomas which, in his opinion, are faults of embryonic beginnings (hamartias).

Lipomas of the fatty capsule are uncommon with the exception of the so-called capsular lipoma, (pages 1311 and 1352). Lipomas weighing many pounds, and fibro- and myxolipomas also occur, leaving the kidney intact, (see Bork, lit.). Frank saw a lobulated lipoma of the capsule weighing 14.2 kgs. Vogelweid (lit.) reported a 55 lb. fibrolipoma undergoing sarcomatous transformation, which, he believed, had arisen from the anterior surface of the fibrous renal capsule. Lipomas within the kidney substance, especially in the cortex, are infrequent; they are often mixed with myomas, (lipomyoma), or sarcomas, (liposarcoma). It is thought that their origin is due to embryological displacement of renal capsular elements. (H. Muller, Nurnberg, lit.)

There occur peculiar multiple tumors situated almost exclusively in the cortex, sharply demarcated, varying in size from the most minute to a lentil-pea-or hazel nut, or rarely, a small apple size; they are grayish white, grayish yellow to yellow in color, soft, or firm, and are foundin both kidneys, frequently coincident with cardiac rhabdomyoma (see p. 84), and tuberous cerebral sclerosis, (in 60–70%). Many small cysts may be present at the same time, as the author has verified. They are mixtures of tissue consisting of fat, smooth muscle and arterial vessels; accordingly, they are spoken of as lipomyomas, angiolipomas, fibrolipomas, etc. The more rare cellular malignant varieties are called liposarcomas, lipomyosarcomas, angiomyosarcomas, etc. They are benign as a rule and give no clinical symptoms. Since uriniferous tubules are absent and glomeruli present in various stages of development, they may be considered tumor-like malformations of renal tissue, or simply tumor-like developmental disturbances, (hamartomas or choristomas). The differentiation from typical mixed tumors of the kidney is made by the absence or paucity of glandular epithelial elements. (See Harbitz, Eller, W. Fischer, lit., Kirpicznik, Kawamura, Bundschuh, Herxheimer.)

Sarcomas have been described even as congenital, and are relatively frequent in children. They often reach immense size. The author saw a sarcoma larger than a man's head in a 2 year old child, and in a 3 year old girl, one weighing 4 kgs. Steinhardt mentions a weight of 13 lbs. in a tumor filling the abdomen. Usually they grow rapidly, are soft, white or pale red, quite vascular and show foci of hemorrhagic softening.

(See Schwers and Wagner, lit., in reference to a rare primary round cell sarcoma of both kidneys in an 8 year old girl; see also Lutembacher.)

In adults we see both quickly growing round cell, and the more frequent firmer, slower growing spindle cell sarcomas. The author has seen tumors varying greatly in size. From hemorrhages, necroses, (clay-colored), cystic changes, myxomatous softening, and fatty degeneration, these tumors may appear exceedingly variegated on cross section. (Resemblance to carcinomas, p. 1389.)

Sarcomas of the capsule are very rare, (see above). Some are angiosarcomas, either alveolar endotheliomas or periendotheliomas in which the vessels are surrounded by spindle cells arranged radially. Ehrmann described an angioliposarcoma.

The congenital renal sarcomas are not, as a rule, pure sarcomas; Kastner's case, in which a spindle cell sarcoma diffusely invaded the whole kidney with the exception of a few remnants, is an unusual one. On the contrary, they are usually of myxomatous structure composed of masses of round nucleated cells, in which are embedded gland and duct-like figures (fig. 722) somewhat resembling uriniferous tubules, sparse, or so abundant as to remind one of adenocarcinoma. There are also lacunae-like glandular distensions (see fig. by Wengraf) which suggest polycystic kidneys. Sickle-shaped and hemispherical cup-like formations strikingly like glomeruli (see fig. by Wengraf) are not rare, but post-embryonal formation of Malpighian bodies does not occur, as is well known. At times spindle cell and myxomatous tissue are mixed with smooth and striated muscle fibres in strands, (Merkel, Hedren, lit.), when they are spoken of as adenomyosarcoma or myosarcoma striocellulare. Fatty tissue, cartilage and bone have also been observed. Birch-Hirschfeld classifies all these renal tumors of childhood into an essentially uniform group and calls them embryonal adenosarcomas or sarcomatous gland tumors; he thinks they originate in fragments of the Wolffian body (primitive kidney,

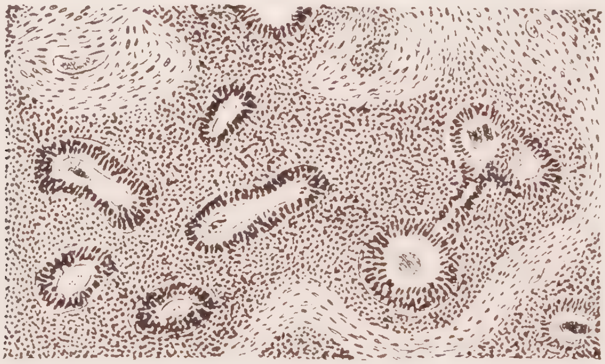


Fig. 722.—Embryonal adenosarcoma of r. kidney of a boy 2¾ years old; weight of kidney, 1340 gms.; gland tubes in rounded nuclear, polymorphocellular sarcoma-like tissue; in between lighter strands of fibrous tissue. (× 150.)

mesonephros) which continue to develop post-partum. He says the glandular tissue is primary and interprets the rounded cells as transition forms which may at any time differentiate into glandular structures. Elsewhere, cell groups may anastomose like carcinoma strands; in other places the structure is more sarcomatous and therefore not of epithelial origin, but archiblastic in nature as in actual mixed tumors. The chief of these tumors is the adenomyosarcoma; in others, one or the other constituent is more prominently developed.

Besides this hypothesis of Birch-Hirschfeld, there are many other attempts to explain these renal myxomas. Of great hindrance is the fact that the embryology of the kidney is still subject to dispute, although the investigations of R. Meyer have cleared up some points. Muus thinks the tumor is derived from the kidney anlage by excessive or irregular proliferation of parts of the renoblast, (p. 1292); thus its sarcomatous, highly nucleated tissue would correspond to the embryonic type with the glandular and muscular elements differentiating from it. Its development, therefore, reaches back to such an early undifferentiated time that all sorts of things are possible, as from the first mesodermic cells. (See also Sand and Lerat.) Wilms places its origin still further back, and assumes there is a scattered displacement of indifferent mesodermic germinal tissue which retains within itself the power to form primordial elements (myotomic cross striated muscle fibres), primordial renoblasts (nephrotomic, gland elements), smooth muscle fibres and various connective substances (sclerotomic or mesenchymatous elements). (See below, by R. Meyer, more details as to this conception.) Ribbert would modify the latter theory in this way: if we assume that they grow from misplaced mesodermic elements in the situation of the future kidney, we might also assume that isolated ureteral buds with epithelial cell caps grow into them and thus the neoplasm is a combination of germinal tissue capable of further differentiation and of already differentiated epithelial cells. Busse believes the tumor is derived directly from the embryonal kidney without help from other embryonal structures, *i.e.*, some of the cells begin an excessive proliferation. Trappe and Sand speak of malignant nephroma. This conception is shared by Aschoff, who considers the primordial kidney theory not proved. Epithelium, as well as interstitial tissue is supposed to proliferate, while cartilage and cross-striated muscle fibres arise by metaplasia from fibromuscular tissue. But Hedren (lit.) thinks that the latter point is doubtful, since such extensive metaplasia has never been proved; he believes in the hypothesis of Wilm for isolated cases. Wengraf, who agrees with R. Meyer, thinks that these tumors are lawless tissue blendings of indifferent mesodermic germinal elements and renoblasts. According to R. Meyer, (see also Merkel's conception), the displacement must be understood as very different from a coarse mechanical process; the explanation for the heterotopy of the elements depends on a lawless union of non-related cells, and displacement is secondary—the consequence of lawless union, because the cells, so to speak, annexed during the slight change in the primitive renal mechanism, are in foreign territory and must adapt themselves, although undifferentiated, to the normal evolution of the primitive renal apparatus with which they are now combined (passive aberration). If such mesenchymal and mesodermal cells (of the myotom or sclerotom) thus reach the primordial renal anlage passively, they must accompany all its changes of evolution, since they cannot reach their own appointed place; the cells of the renoblasts form the glandular elements of the new growth. But the misplaced cells lose none of their potentialities in their new situation and thus give rise to the different tissues found in the tumors, (p. 1392). Briefly, the question of genesis is still under discussion, but the hypothesis of Birch-Hirschfeld may be considered as disposed of. (See R. Meyer.)

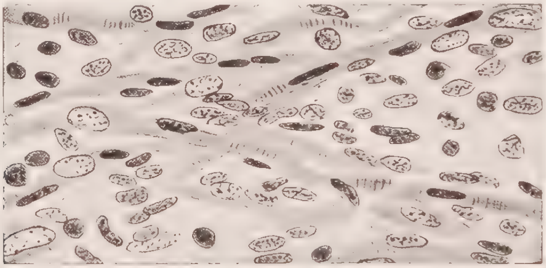


FIG. 723.—Rhabdomyomatous portion from a large embryonal adenosarcoma; girl 4 years old. In between sarcoma cells of various forms. (High power.)

Embryonal adenosarcoma is the typical malignant tumor of the kidney of childhood, and probably most of the renal tumors of children described as sarcomas or carcinomas belong to this type. In a baby 3 months old, the author saw an adenosarcoma of the right kidney the size of a man's head, and he reported 3 cases (C. f. Schw. 17, 1906) of this kind in which the chief characteristics were well marked, viz., quick growth, and absence of hematuria. (See K. Schneider.) As a rule they are unilateral, but have been observed in both kidneys, (lit. by Merkel). Occasionally we see them in adults, even in the sixth decade. (Hedren.) Rohde described a malignant mixed tumor in a man 57 years of age, which he considers derived from misplaced mesodermic and ectodermic cells. Bauer saw carcinomatous and sarcomatous metastases.

Secondary sarcomas usually form rounded, sharply demarcated nodules, sometimes very numerous. Occasionally, leukemic lymphomas have a quite similar appearance, (comp. p. 1374).

The author saw an 8 year old boy with acute lymphatic leukemia and a hemorrhagic diathesis, whose kidneys weighed 136 and 132 gms. and were filled with rounded, soft, almost white nodules with their contours somewhat vague, but quite prominent in the cortex. In a woman 34 years of age with acute myeloblastic chloroleucemia, the kidneys were filled with numerous small rounded nodules, especially in the cortices. In both cases the nodules were not sharply demarcated from the surroundings! (Compare with metastatic sarcoma.)

According to Recklinghausen, tumor metastases in the kidneys may also be implanted by retrograde venous transportation (p. 169), when carcinoma or sarcoma fragments are carried from the inferior cava into the renal veins, or grow into them. Teratomas (of testis or ovary) may penetrate the vena cava or renal veins, and from there infiltrate the renal tissue and even become visible on the kidney surface. (Consult metastatic teratomas, p. 1390.) In a 21 year old girl with malignant ovarian teratoma, the author saw immense metastases to the abdominal lymph nodes and liver, while a large tumor projection continued into the inferior vena cava and renal vein; tumor masses had densely infiltrated the kidney.

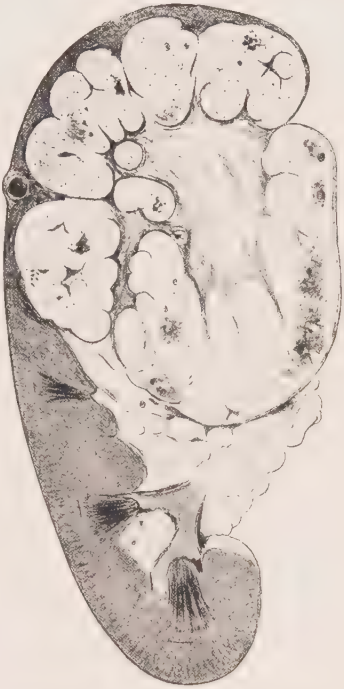


FIG. 724.—Hypernephroma of r. kidney of man 74 years old. The tumor was yellow white to yellow and spotted red; the central fibrous part light blue gray; kidney tissue brown red. Weight of this kidney 180 gms.; of the left, 192 (!) gms.; ¾ nat. size.

Aberrant Heterotopic Hypernephroma. (Struma lipomatodes aberrata renis.) P. Grawitz designated with the latter name benign renal neoplasms which he considered due to a proliferation of misplaced adrenal tissue, which had been snared off during embryonal development of the kidney (p. 1281).

It was admitted, however, that an adrenal nature of the tumor may be claimed for only some of the cases, and therefore, the suggestion was made that they be designated simply as Grawitz tumors, (W. and W. Gerlach), although some workers differentiate between Grawitz tumors and nephrogenous neoplasms, (Stoerk, p. 1398). Both may be macroscopically similar (Ribbert). Generally speaking, the name "hypernephroma" is to be preferred.

Two main groups may be differentiated: (*a*) benign, (*b*) malignant. The former are usually small tumors, of the size of a cherry, or walnut, sulphur yellow, rounded, or slightly angular, mostly situated within the cortex near the periphery and bulging more or less into the capsule, sharply defined with typical architecture. They frequently have a definite fibrous capsule and usually make their appearance in older individuals. Larger nodules may show a hyalin fibrous centre from which branches radiate; they are frequently of variegated color due to hemorrhages. The malignant form is recognized by invasion of veins, pelvis, penetration of the tumor capsule, infiltrating growth, and frequently by extensive metastases. A typical form which, similar to the benign type, has a capillary network with its meshes filled with cells containing fat and glycogen, may be distinguished from an atypical, more rare form, which resembles the corresponding adrenal tumor, (p. 1290). There are transitions between both.

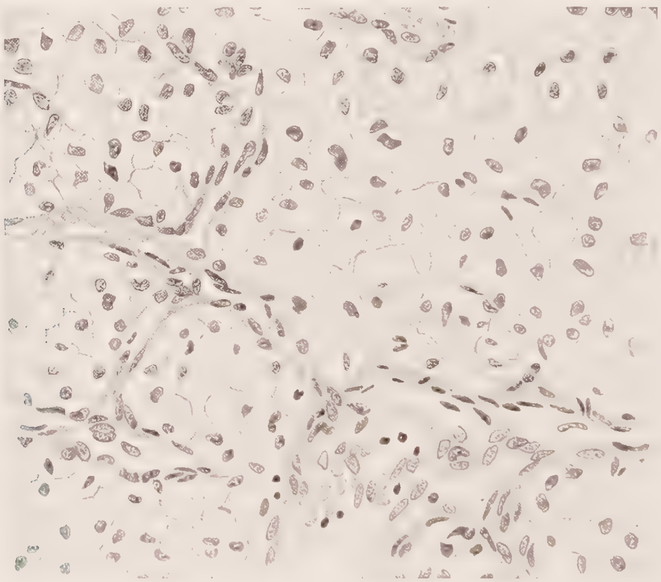


FIG. 725.—Malignant typical hypernephroma of a kidney of a woman 58 years old. Capillary blood vessels form a scaffolding in which are lying transparent cells as in a mosaic. Tumor masses had invaded both veins and pelvis and formed metastases. (High power.)

The designations, typical and atypical, refer to the histological structure, which in the one case is similar to adrenal architecture, in the other case, dissimilar. Considered biologically, a typical renal hypernephroma may be either benign or malignant, depending on whether it is aggressive, penetrates vessels, and produces metastases. An atypical hypernephroma, on the other hand, is malignant *ipse facto.* (Comp. typical and atypical varieties of chorio-epithelioma.) Some clinicians consider the majority of hypernephromas malignant, (lit. New).

Hypernephroma is "the" typical renal tumor of middle or advanced age. In 215 cases by Paschen, 74 occurred in the fifth decade, 81 in the sixth, 30 in the seventh; 146 were in men, and 69 in women. The size varied from a chestnut to a man's head and over, when they weighed several kilos. In a woman of 29, the author saw tuberculosis in the same kidney.

Most sarcomas of the kidneys of children (see above) have been wrongly classed as Grawitz tumors, whereas, they are adenosarcomas.

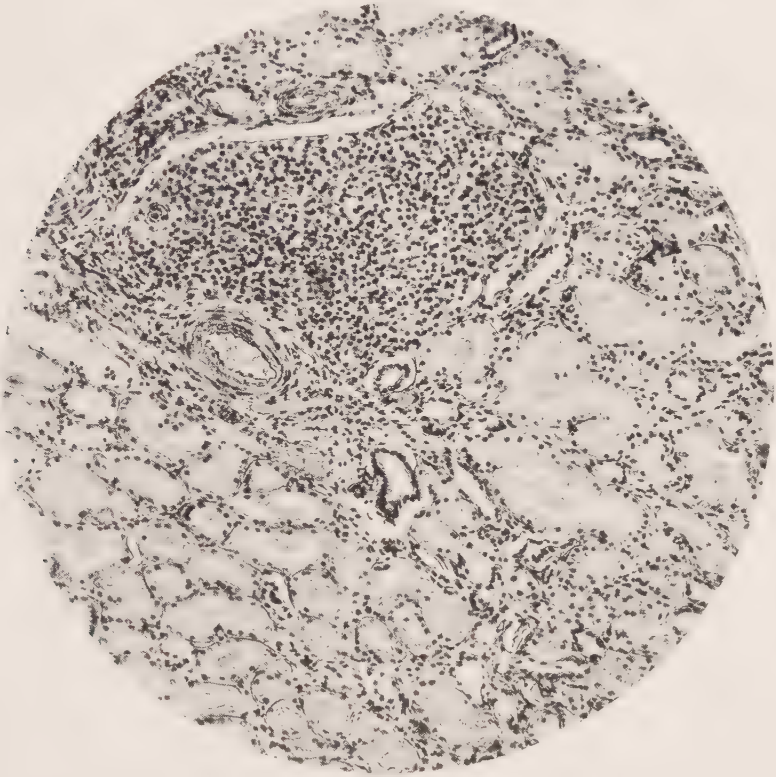


FIG. 726.—Nodule in the cortex of the kidney of a man 70 years old. This nodule was discovered in the course of the routine examination of sections obtained at autopsy. The exact derivation of the cells of the nodule is of course not known but in all probability, they are embryonal. × 120. L. H. #1097.

Microscopically, the benign typical hypernephromas contain a delicate stroma as in the adrenals (p. 1287), consisting practically only of capillaries among cylinders and groups of the large polygonal cells, many of which are filled with fat droplets. Gland-like lumenae also occur, (lit. by Askanazy, Beckmann). Sometimes two or three zones are recognizable as in the normal adrenal cortex. But not rarely an unusual structure (in reference to adrenal tumors, but occurring in these too, according to Kostenko) is predominant, *i.e.*, a papillary architecture. Hypernephromas usually are very rich in glycogen which gives the cells a foamy, honey-comb-like protoplasm, or a transparent appearance as in plant cells. Blood spaces sometimes resemble cavernous angiomas. Hemorrhages, necroses and softening cause red and brown discolorations and cyst-like cavities. Since the malignant typical hypernephromas show the same adrenaliform histological structure (fig. 725) as the benign, it is essential to examine the extirpated kidney as to its veins (invasion, tumor thrombi), and its pelvis (invasion?), to arrive at an estimate of its malignancy. In the atypical malignant hypernephromas, the structure is quite lawless. (See page 1290.)

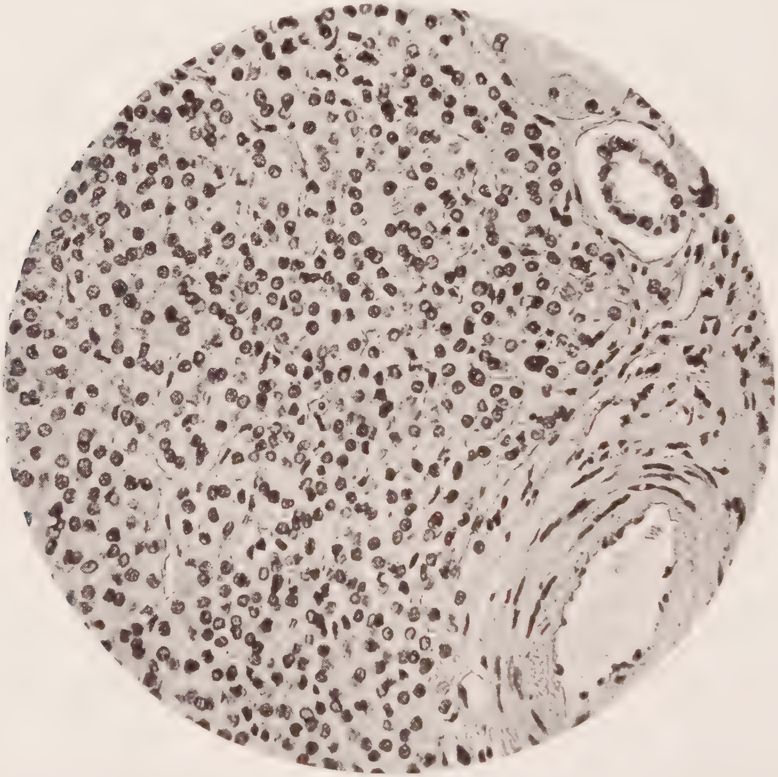


Fig. 727.—Showing more details of the cells and their arrangement in the nodule in the cortex of the kidney. It takes little imagination to recognize a similarity between these cells and their arrangement and the cells of the adrenal cortex. The relation of such nodules to tumor formation is discussed in the text. × 260. L. H. #1097.

Stoerk supported the theory advanced by Sudeck, actively opposed by Lubarsch, of the nephrogenous nature of the Grawitz tumors; according to him they are epithelial tumors of a tubular character (adenomas or papillary cystomas, *i.e.*, carcinomas), and have nothing to do with misplaced adrenal tissue. Previous to this Sabolotnow (institute Marchand, lit.) had supported the theory of adrenal origin, (see Clairmont); Neuhauser, in his last implantation experiments, obtained, in accord with Schmieden and in opposition to Stoerk and v. Haberer, adrenal tumors which looked like Grawitz tumors in the kidneys of rabbits. Zehle also speaks of nephrogenous origin and believes that these tumors arise from compensatory hyperplasias, which however seems doubtful. While Steinke is more convinced than ever of the truth of the old conception of Grawitz's tumors after investigations of adrenal tumors in

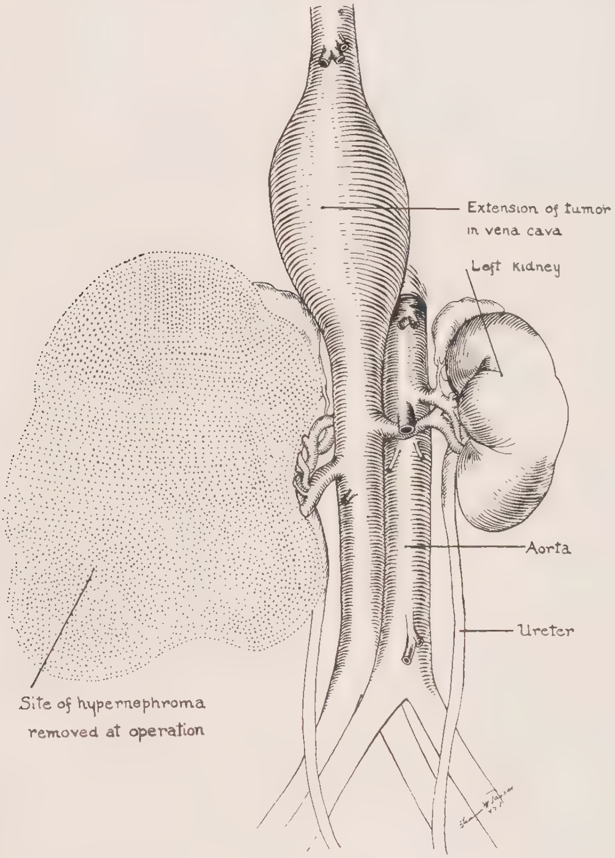

Extension of tumor in vena cava
Left Kidney
Aorta
Ureter
Site of hypernephroma removed at operation

FIG. 728.—Diagram to show position of right kidney completely replaced by hypernephroma. This mass was removed at operation. The patient, male 50 years old, died of cardiac failure ten days later. At autopsy a huge tumor mass was found in the inferior vena cava almost completely obliterating the vessel. There was, naturally, excessive passive congestion of the parts drained by this vessel. There were a few scattered, small metastases in the lungs but the tumor in the vessel extended as far as the right auricle. This is not an uncommon condition in hypernephroma. It explains the wide-spread metastases which these tumors are apt to produce. The condition was suspected at operation because of the consistency of the vessel which was felt as a firm cord, but the operation was necessarily continued because of technical surgical reasons. Patient's symptoms dated some six months.

cattle, Sissen, after comparing true adrenal tumors in animals, justifies the doubts of Stoerk. Gelle considers it an open question, (see also Brault and Courcoux, lit.); Kostenko supports the old conception. Willis, in contradistinction to Stoerk, would have us believe the tumors originate in the primitive renal blastoma, (Wolffian origin, see Wilson, who speaks of mesothelium), and considers the differences too many between hypernephromas and malignant epithelial renal tumors to allow of complete identity. Still he thinks it conceivable that both tumors originate from the remnants of a former mutual germinal anlage for the production of both kidneys and adrenals, from which sometimes more adrenal, at other times more kidney-like forms develop, an explanation Herxheimer considers plausible. Glynn too, for various reasons, denies the application of the Grawitz theory in most cases; the renal nephromas, in contradistinction to those of the adrenals (p. 1291) never influence sex characteristics. Ipsen, Herxheimer, Hartung, Lindstrom and others have accepted Stoerk's ideas. Rosenfeld (Dietrich) takes the middle ground and differentiates: (*a*) tumors of hypernephroid character (Grawitz tumors); (*b*) papillary cystomas and adenomas according to the Grawitz type (Stoerk); (*c*) papillomas and adenomas of renal cell type; (*d*) carcinomas. (*a*) and (*b*) are said to occupy a separate place among kidney tumors, for, especially in type (*b*), their genesis has never been demonstrated, *i.e.*, from renal epithelium or from adrenal cells.

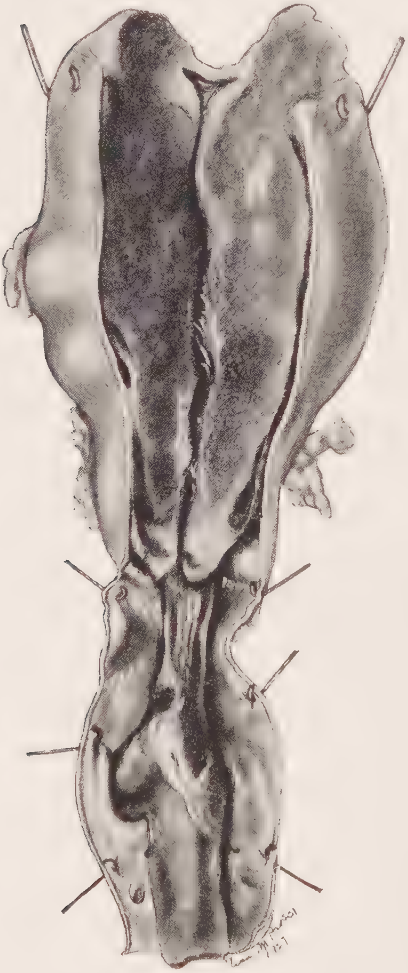


FIG. 729.—The inferior vena cava from the case fig. 728 opened to show tumor mass within the lumen.

General Characteristics of Malignant Renal Tumors.—Invasion into the veins is quite frequent (see Sutter, lit.); even in small children, a tumor the size of a finger is sometimes found in the renal vein, and may continue into the inferior cava and possibly into the heart itself, (*e.g.*, cases of Oberndorfer, Merkel, lit., Kirschner, French). Metastases follow, especially to the lungs and liver; they are more frequent in carcinomas and hypernephromas, and relatively rare in the adenosarcomas of children. They may appear after a number of years (Paschen, lit.). In a 39 year old man, whose left neoplastic kidney (malignant hypernephroma, clinically) had been removed 6 weeks before, the author saw numerous metastases to the lungs with invasion of the pulmonary veins, and numerous small nodules, almost all cortical, in the right kidney, nodules in both adrenals, liver, brain cortex, and in the fifth thoracic and first lumbar vertebrae. Metastases of malignant renal hypernephromas occur in the skeleton relatively often, (see lit. p. 1225). The regional lymph nodes are sometimes infiltrated. Metastases may give the first clinical symptoms; thus, when in the skeleton, there may be spontaneous fractures, compression of the spinal cord, etc.; they may be found first in the inguinal nodes, brain, etc., (see Simmonds, Benesi, Angstein).

Thrombosis of veins within the tumors often occurs and sometimes accounts for extension to the trunk of the renal vein when the tumor grows into the blood thrombus. Varicocele, due to occlusion of the spermatic vein (pressure from lymph nodes or tumors), may be an important clinical symptom, (see Hochenegg). Invasion of the tumor into the pelvis is also frequent. Tumor masses like plugs or polyps block the ureter. Dead tumor particles may become concretions.

Malignant tumors, especially those in adults, rupture early through the fibrous capsule (Kuster); the author saw this occur in a 24 year old girl with malignant hypernephroma which ruptured into the colon and became extensively infected. It may extend into the adrenal gland.

Changes in the Situation of the Abdominal Organs from Large Renal Tumors.—Large tumors of the left kidney usually lift the descending colon so that it is pushed upward from the left, and passes downward between the tumor and the anterior abdominal wall toward the right and beneath the tumor. This can be proved by percussion, (they may be confused with retroperitoneal tumors, see fig. 426). Tumors of the right kidney displace the ascending colon from the right below, toward the left above.

Clinical Symptoms.—The urine may be unchanged, particularly in children in whom this is almost the rule, and the first symptom is the palpable and usually visible tumor. On the other hand, in adults, according to Albarran and Imbert, hematuria is the most frequent symptom of renal tumors, by no means only from histologically malignant growths; It is said to be the primary symptom in 54%, or according to others, in 70% of cases, (see Garre', Borchard, Albrecht). The passage of worm-like blood coagula may stimulate the colic of renal calculus. Later, local pain and a palpable tumor appear. The extent and locality of the tumor within the kidney substance seem to have but little influence on the appearance of hematuria. The author, for instance, saw massive hemorrhages warranting extirpation of the kidney in a man 60 years old with a hypernephroma the size of a chestnut. For other clinical details see Beilby, Franck, Kummell. Generally speaking, the prognosis in malignant renal tumors is relatively favorable if early operation is performed.

Parasites of the Kidney.—The most important animal parasite of the kidney is the echinococcus, sometimes with quite large cysts. Rupture and evacuation into the pelvis are followed by the passage of hooklets, scolices and fragments of the striated membrane in the urine. Pyemia has been known to follow infection of the cyst.

Distomum hematobium (p. 856), may establish itself in large numbers in the mucosa of the pelvis, the ureters and bladder, causing inflammation, ulceration and possible polypoid growths (details, p. 857). The ova appear in the urine (fig. 20, p. 849).

Filaria sanguinis hominis, (fig. 114, p. 211), causes hematochyluria, so that the urine appears almost like milk from the presence of fat droplets. Hematuria is apt to be combined. Lymph sacs may rupture into the pelvis.

Eustrongylus visceralis is rare in man. It locates in the pelvis and causes marked destruction of kidney substance, dilatation and areas of calcification in the pelvis, (see Blanchard, Brumpf).

Cysticerus cellulosae (p. 848) and **Pentastomum** (p. 978) are without importance, and quite rare.

Trauma of the Kidney.—Traumatic rupture is more frequent of the right organ; apart from bullet wounds, (see Kummell), it is rare from such direct trauma as a horse's kick, which usually ruptures the liver at the same time. It is more likely to happen through a fall, or by being caught under falling material, being run over, etc., especially in children. Transverse tears are more common; they run perpendicular to the long axis, and usually start from the hilum, the direction being due to the anatomical structure of the kidney, rather than to its form of attachment, thus differing from the liver, (see Geill). Penetrating bullet wounds often cause extensive infarction (Dietrich and others), and the hemorrhage may be fatal (lit. by Wagner). The healing of ruptures or operative incisions (nephrotomy) is by connective tissue. (See Lobenhoffer.) See Thorel, lit., for regenerative processes, such as reunion of straight tubules by anastomosis; also Orth for traumas and renal diseases.

Appendix.—Spontaneous massive hemorrhages, the so-called apoplexy of the renal bed (Doll), occur suddenly with acute pain. The dense, elastic, massive hematoma, several centimeters thick, may be peri- or para- renal. In the perirenal form the blood lies between the kidney and its fibrous capsule; in the second form it is outside the capsule. They are considered due partly to rhexis, and partly to capillary diapedesis from loss of stimulation by the vaso-motor apparatus. (Ricker.) In one case, E. Koch thought the source of bleeding was in the adrenal. (Lit. by Coenen; Lawen, Kummell, Schlichting, Bollay, H. Schultze, Sohn.) Lehnert, (lit.), described a sclerosis of the renal bed caused by this process; the fat capsule showed numerous hemorrhagic foci and was penetrated in various directions by connective tissue strands.

PELVIS AND URETERS

MALFORMATIONS (see page 1296)

Hydronephrosis.—(**Hydronephrotic atrophy of the kidneys.**) When the outflow of urine is hindered anywhere below the pelvis there is stasis above the obstruction carried backward into the pelvis. The resulting uni- or bilateral dilatation of the pelvis is called hydronephrosis (hydronephros, according to Aschoff).

The first symptoms of obstruction, no matter what the cause, are felt in the kidney itself; stasis of urine in the tubules is responded to by polyuria, (for more details, see under hypertrophy of the prostate).

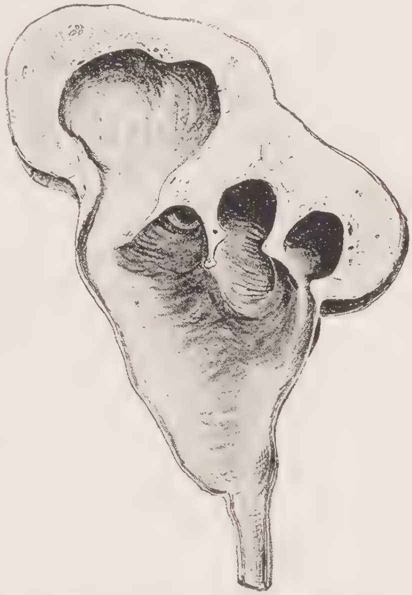


FIG. 730.—Hydronephrosis; longitudinal sect. through specimen hardened in chromic acid; $^2/_3$ nat. size.

The pressure from the pelvis flattens the pyramids, the calices become dilated and spherical in shape, thus altering the direction of the tubules so that they are arched or horizontal. Soon the pyramids and medulla are hollowed out, and finally, the cortex is pressed flat and dilated toward the periphery. Externally, the enlarged kidney first shows spherical prominences representing the dilated calices, but as the dilatation increases, the kidney becomes a knobby, thin-walled sac from which the parenchyma may finally disappear to mere traces. The internal surface of of the sac is flat, glistening, and white, the septa dividing it into a number of compartments are either remnants of the columns of Bertini, which originally separated the pyramids, or thickened larger blood vessels which coursed between two calices.

A hydronephrotic kidney is very frequently two or three times larger than a normal kidney, occasionally as large as a child's or man's head, or, exceptionally, as large as an extreme ovarian cyst (fig. 731), for which it may be clinically mistaken; the sac may contain 10 to 12 liters of fluid. Under other circumstances, the kidney with the pelvis may be smaller than normal. If bilateral, death results from uremia; if unilateral, the other kidney may enlarge; *e.g.*, a kidney examined by the author weighed 290 grams (31 year old man with severe pulmonary tuberculosis).

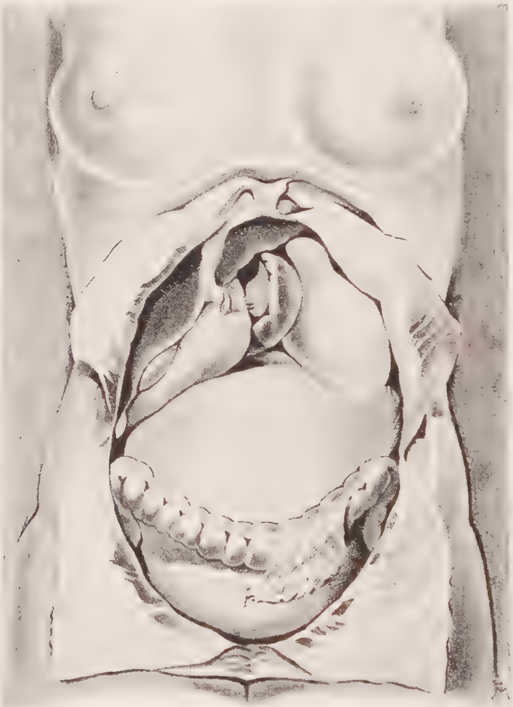


Fig. 731.—Very advanced left hydronephrosis due to insertion of ureter in pelvis at an acute angle. Opening the abdomen exposes an immense, lumpy, subperitoneal watery translucent sack, 30 cm. across; at its highest point is the transverse colon and omentum. The spleen is pushed toward the midline; to the right, the stomach below the liver; behind and below the stomach the loops of the small bowel; a continuation of the sac as large as a child's head forced into the pelvis compressed the r. ureter. Woman of 33 with pulmonary phthisis.

In a 45 year old woman, the author saw a rather uncommon condition in which the sac was almost as large as a man's head, but the kidney itself had been very little dilated; the sac was like a diverticulum from out the hilus; the author has seen similar pictures in children. Morgenstern described a giant diverticulum of the pelvis in carcinomatous stenosis of the ureter.

In traumatic stenosis of the ureter near to the kidney (lit. by Wagner, Pleschner, Lunden), the later hydronephrotic sac may rupture, (true traumatic hydronephrosis), and after the fatty capsule has been lifted, inflammatory connective tissue may form an enormous new sac. These pictures are quite puzzling. The author saw such a pararenal hydronephrosis, traumatic pseudo-hydronephrosis of the left kidney, in a 50 year old man after the left side of his abdomen had been crushed by a wagon wheel. A traumatic hydronephrosis may also develop from the pressure and shrinkage of a perirenal and periureteral hemorrhage which obstructs the ureter (Wagner). See also Picard. (Consult v. Saar, Babitzki, Albert, Brentano, concerning the rupture of hydronephroses.)

But a so-called perirenal hydronephrosis may arise from mere separation of the fibrous capsule (by edema, Minkowski), with subsequent accumulation of fluid (rare). Such intracapsular hygromas of the kidney (Ponfick) may be due, furthermore, to perirenal hematomas, (Coenen, see page 1403); see also Hagemann, Wrede.

If the obstruction is below the ureters, these become more or less dilated, thin and transparent, and take a serpentine course. When unilateral, the dilated ureter may be quite enormous. Thus, in an old prostatic, the author found the left ureter dilated to the diameter of a filled loop of bowel; it lay on the left iliac bone as a water-clear, translucent, s-shaped structure felt as a tumor through the abdominal wall. Saccular hydroureters may also be due to congenital obstructions which have not been manifest until later years, thus, in the cases of Oehlecker and Brutt, at the time of puberty.

Occasionally, the papillae undergo necrosis without the intervention of bacteria (Chiari); consult p. 1364.

In the early stages, there are microscopic atrophy, cloudy swelling and mild fatty degeneration of the cells of the tubules and glomeruli, with many casts and much albumen in their lumena. The tubules in the pyramids are often pressed together like harmonicas; later, there appears a chronic interstitial inflammation. (The same conditions were seen by Joest and his co-workers in the hydronephrosis of swine.) In fig. 732, a very advanced stage, some of the glomeruli are merely small, others are in various stages of destruction and shrinking, many are surrounded by thickened capsules and lie so close together that a large number appear in any one microscopic field. Here and there atrophic tubules are seen, with many a-cellular spaces and thickened vessels, embedded in a richly cellular connective tissue. Other arteries and veins are also thickened. As Orth points out, the glomeruli lying loose in their capsules retain their structure for a surprisingly long time, (as in the experiments of Ponfick); finally, however, they disappear (figure 732), are hyalinized, and adherent to their equally hyalinized, thickened capsules (Zurhelle, lit.). Sometimes it is quite difficult to harmonize the marked contrasts in the parenchyma; between destroyed parts are others in which even hypertrophic compensatory changes in both tubules and glomeruli have taken place, due perhaps to varying resistances to the pressure of different calices, and perhaps also to varying conditions of the elastic fibers of the pelvis, which may be increased in number (Oertel). This is significant of the functional capacity of the kidney, when the cause, *e.g.*, kink of the ureter, hypertrophy of the prostate, etc., is removed by operation.

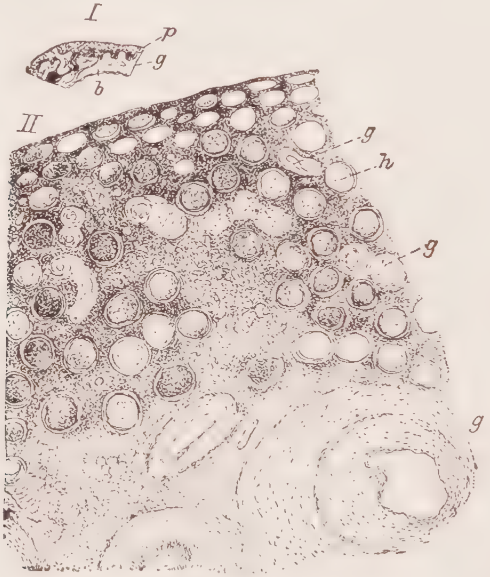


FIG. 732.—Hydronephrotic atrophy of kidney; I. portion of a marked hydronephrosis. whole thickness of wall of sack, nat. size; p, parenchyma; g, vessels; c, pelvis. II. From same kidney; h, glomeruli; partly hyalin, mostly loose in capsules; g, blood vessels very markedly thickened; in cellular interstitial tissue here and there atrophic tubules. (Med. Magn.)

Thickening of the vessels is due in part to inflammation, just as are the changes in the vessels in other interstitial inflammations; to a large extent, however, there is also an hypertrophy from increases in pressure, which in the veins, is due to stasis in front of increased pressure of blood in the arteries. For the same reason, hypertrophy of the heart is developed in hydronephrosis.

In a soldier with left hydronephrosis, the author found that the left renal artery would allow passage of nothing but the finest sound; the right kidney weighed 275 grams, and its artery allowed the passage of a lead pencil.

In the beginning of hydronephrosis, the content of the sac is composed of typical urinary substances such as urea, uric acid, etc., in addition to albumen. In time, however, its urinary character is lost, probably from resorption through lymph vessels; it then contains an albuminous fluid derived in part from the vessels (glomeruli) as a transudation from the blood, and in part as a secretion or exudate from the mucosa of the pelvis, analogous to hydrops vesicae felleae. Occasionally the contents are thick, colloid, bloody, chocolate-like or cholesterin-containing.

The causes of hydronephrosis may be:

Congenital.—When the opening of the ureter into the pelvis is lateral, or at an acute angle, marked filling of the pelvis may lead to valve-like closure of the ureter (valvular hydronephrosis); this type of obstruction may be intermittent. But Bazy believes the cause of this intermittent hydronephrosis is a particular congenital arrangement of the pelvis (large pelvis of a horizonital type) combined with ptosis and abnormal mobility of the kidneys; the latter may then produce annular or linear retractions, torsions and folds of the ureter. Such valvular hydronephroses are, in all probability, due to an unequal development of the parts of the pelvis, and may appear in intrauterine life; thus in a 15 day old child, the author found a hydronephrotic kidney as large as that of a similar condition in an adult. Congenital stenoses and atresias of the ureter (page 1296), or of the urethra, or a diverticulum in the bladder end of the ureter, which pushes into the latter structure, are occasional causes; furthermore, abnormal relations of vessels to the hilus of the kidney, usually on the right side, more frequent in males, may cause hydronephrosis; thus the main branch or branches of the artery or the vein or the spermatic vein, or accessory vessels at either pole, may cross the ureter (see Ekehorn, Merkel, lit., Klukow, lit., Hutchinson, lit., Liek). This may be in front or in back, and thus lead to difficulties in emptying the ureter, or even produce valve-like closure, especially in acute angular insertions of the ureter. See Ahrens, concerning hydronephrosis in horse-shoe kidneys. Even phimosis of the prepuce may lead to very grave hydronephrosis, often quite latent, until death occurs from uremia (see, among others, Heinrichsdorff).

Acquired.—There may be mentioned: urinary stones in the pelvis, in the ureters, or in the bladder. Ponfick believes that most hydronephroses occurring during the first year of life, are due to dilatations behind small concrements in the urinary tract. Primary tumors of the pelvis, of the ureters (very rare), of the bladder, tumors and benign so-called hypertrophies of the prostate, larger tumors of the abdominal cavity, *e.g.*, ovarian cysts, uterine prolapse (consult Hirokawa), may all lead to hydronephrosis. It may also arise from traumatic scars, inflammatory tuberculous stenoses of the ureter (the author saw tuberculous stenosis in the upper part of the right ureter in a boy 11 months old), gonorrheal strictures of the urethra. Tumors secondary in the bladder or ureters, *e.g.*, from carcinoma of the uterus, frequently produce hydronephrosis and uremia; occasionally there is amyloid in the kidneys; furthermore, in stomach or gall bladder carcinomas, a ureter is stenosed through pressure of masses in the peritoneum and the abdominal lymph nodes, and occasionally, though more rarely, nodules and infiltrates develop in the ureteral wall itself. Changes in position, tearing of the kidney, or the ureter, *e.g.*, in high grade kyphoscoliosis, or torsion of movable kidneys may lead to hydronephrosis by folds, valve formations, or kinks, (compare movable kidney, page 1298). For experimental hydronephrosis, see Ponfick, Winkler.

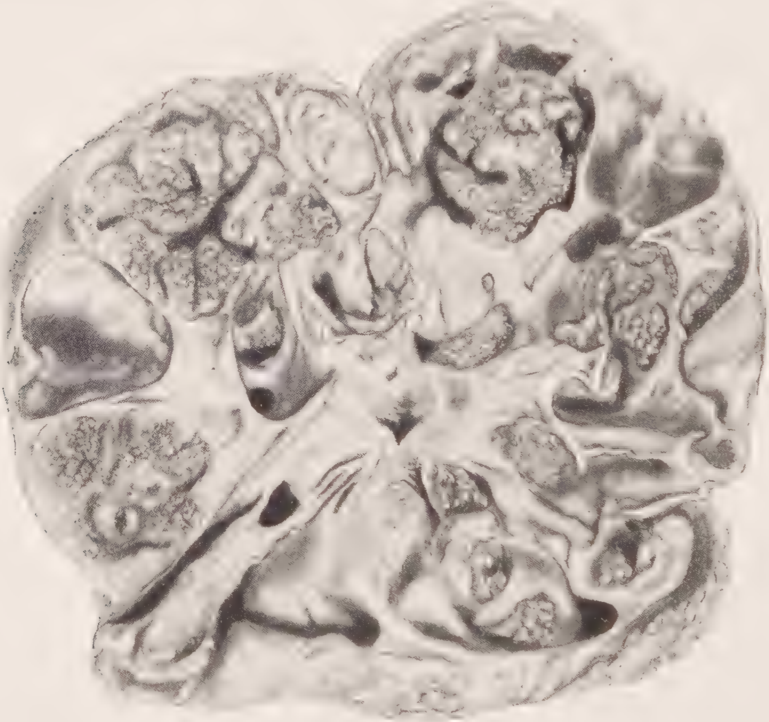


FIG. 733.—Hydronephrosis and metastatic carcinoma of the right kidney; primary tumor in the bladder. L. H. #5. ⅖ nat. size.

It may be mentioned that the causes which produce hydronephrosis are never able to produce a cystic kidney (page 1382, see also Orth, Ruckert), but cystic kidneys and hydronephroses may be combined.

In intermittent hydronephrosis, the stasis of urine in the pelvis and in the ureter is caused by temporary, but recurring obstructions such as renal or ureteral stones, dislocations of the kidneys, primary and secondary changes in the ureter (page 1296), compression or displacement of these organs, traumas, etc., (see Michalski). Bazy has hunted for a cause in congenital malformation of the pelvis (large pelvis of horizontal type), in which retractions, torsions and folds are possible in the upper part of the ureter.

See page 1296 concerning cystic dilatation of the bladder ends of the ureters.

The Formation of Concrements in the Kidneys, in the Pelvis and in the Ureters

Nephrolithiasis.—Kidney stones may originate in the pelvis or the calices or the kidney itself, and may increase in size in the pelvis. They are usually unilateral, more frequent on the right side (compare Hess, Siedamgrotzky), but are occasionally bilateral. According to size there are differentiated: (*a*) pulverized kidney sand, (*b*) larger particles of kidney gravel, which appear like rough sand—both of these forms may easily pass through the ureter, and are composed mostly of uric acid and its salts, (*c*) kidney stones or larger concretions. The number, size

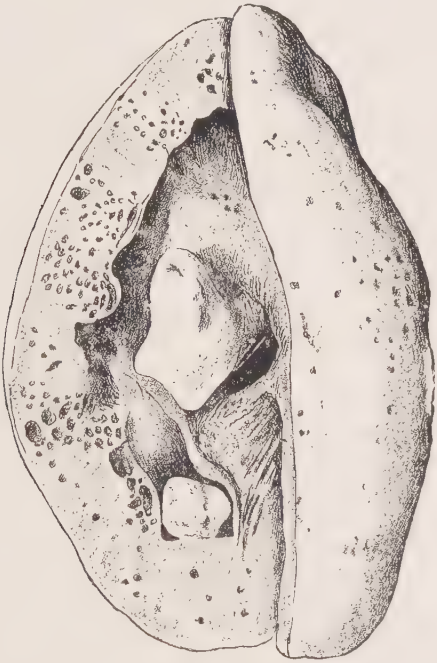
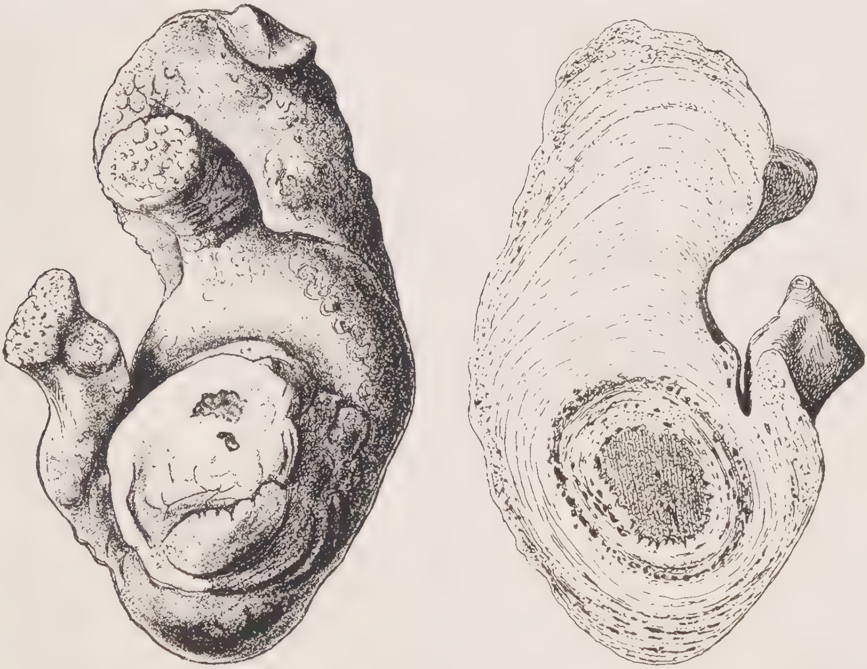


FIG. 734.—Calculi in pelvis. After cutting through kidney, two calculi (urate) in the pelvis, the largest partially blocking the ureter; numerous abscesses appear as holes in the alcohol preparation. (Calculous pyelonephritis.)

and weight and chemical compositions of the latter are extremely varied. In Gottingen there is one weighing 267 grams, and Dietrich saw a stone weighing 550 grams. Most kidney stones, however, are as large as millet seeds to peas. Larger stones have differing contours; some are pronged and branched, and occasionally fill the pelvis like a cast (fig. 737); others are like coral or antlers; others are pyramidal; if a number of stones are present their surfaces are usually facetted, (fig. 737).

General Observations Concerning the Origin of Urinary Calculi.—As the investigations of Ebstein, Posner and others have shown, the stones which are found in the kidneys, pelvis, bladder, even in the urethra and in the prepuce, and which frequently are washed down from above to a lower position, are not formed from simple precipitation of calculus material. There must be added one or several conditions: (*a*) an organic framework which is called the albuminous stroma (Ebstein), the albumen coming from the kidneys themselves as in a uric acid infarct, or from the urinary passages, and differing from that in normal urine. The latter statement, however, has been shown to be incorrect, because every stone and every sediment in otherwise normal urine has a scaffolding (Pfeiffer, Moritz, Schreiber, Aschoff). According to the newer viewpoints, particularly those of Lichtwitz (lit.), this scaffolding comes from colloid precipitation in the urine. There are both albuminous and non-albuminous colloids present. (*b*) To these are added stone-forming substances precipitated from the urine, not usually in a pure state, but mixed in varying proportions with other substances, and not in simple form, layer upon layer, but settled into the framework and encrusted in its meshes. (*c*) As the experimental introduction of foreign bodies elsewhere has demonstrated, dead masses of tissue such as shreds of epithelium, blood, mucus (in catarrhs), fibrin, pus, the ova of distomum, and bacteria, may be the primary point of origin of calculi, *i.e.*, if a true concrement is to be formed, masses of albumen precipitate around these foreign bodies which then act as nuclei. According to this newer viewpoint concerning colloids (Lichtwitz), all these bodies have the general physical quality of presenting strange surfaces in the urine. The coagulated colloid attached to the surface forms a sort of skin which is encrusted by crystalline substances in the urine. The calcified or stony layer in its turn, acts again as a strange surface. Since the process of colloid precipitation and incrustation is repeated over and over, a laminated stone results different from ordinary sediment (see page 1414). According to Kleinschmidt, on the other hand, crystallization is the primary process; the precipitating crystals pull down the albumen with them, and by diffusion in the separated salts they make the albuminous scaffolding. Schmorl found small, or larger, soft concrements composed of practically nothing but bacteria enclosed in a laminated layer of albuminous material (see also Jores). Concerning the actual causes of nephrolithiasis, nothing whatever is known. The stone-forming diathesis may be familial and inherited; some of the members of one family may have gout, others have lithiasis, and others have both. It is a matter of experience that nephrolithiasis is frequently observed in metabolic disorders, particularly gout (page 1252), even though the gouty individual may excrete low amounts of uric acid, while in urolithiasis the reverse is usually the case.



Figs. 735 and 736.—Large renal calculus with thick prolongations; longitudinal section of one with nucleus of urates and massive covering of earthy phosphates; dry weight 93.1 gms.; from a case of squamous cell carcinoma of left pelvis (and local lymph nodes); nat. size.

The statement, however, that lithiasis is a symptom of gout must be contradicted for several reasons, (compare Lichtwitz who believes the general cause of both resides in the kidney; see also M. B. Schmidt, lit.). The disease is more frequent in males than in females. Children are frequent sufferers, and the importance of uric acid infarcts in the newborn (page 1375), which is a sediment formation in the kidneys, is unquestioned; the kidney and bladder stones of adults often date from childhood (Mousseaux). Unilateral nephrolithiasis may be combined with developmental disturbances of the kidney, or of the pelvis, or with tumors. Local causes are then probably of etiological importance. Infection of the urinary passages with decomposition of the urine may favor stone formation; (compare under stone formation following injuries of the spinal column, the spinal cord and paralysis of the bladder).

From the chemical viewpoint the most important components are as follows:

1. **Urate stones,** composed of pure uric acid or uric acid salts (Na, NH_3, Mg). These are the most frequent, are of moderately hard consistency, with soft or granular or nodular surfaces, yellow-brown or red-brown color. On fracture, they are usually found laminated. A necessary factor in the formation of uric acid stones is a very acid urine. According to Kahn, pure uric acid stones are quite rare; calcium oxalate is usually added. Uric acid stones soften in formalin, and therefore may easily be cut for microscopic study (Orth). The murexid test with ammonia gives a purple red color, and a purple violet color with liquor potassae.

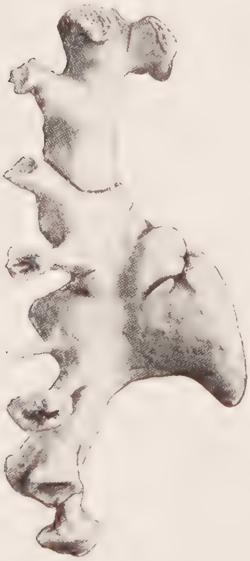


FIG. 737.—Pronged renal calculus (urates with phosphate coating); a cast of the calices and pelvis; ⅞ nat. size.

2. **Oxalate stones** are composed of calcium oxalate, are very hard, usually small, warty, mulberry-like, stellate, have a tendency to injure the mucous membrane, of themselves are colorless but are often stained by hematin to a light or dark brown or black brown color. The fracture surface shows radiations. These stones are rarely pure, and are often covered by a layer of uric acid (fig. 747); in fact, calcium oxalate and urates may be present in alternate layers. These stones are also formed in acid urine; (in animals, Ebstein and Nicolaier produce oxamid concretions after feeding oxamid). The crushed powder effervesces on addition of hydrochloric acid.

1 and 2 are very often mixed.

Pfister (lit.) calls attention to the predominance of oxalate stones in Egypt and in India, while in China, *e.g.*, uric acid stones are much more common.

3. **Phosphate stones,** composed of the salts of phosphoric acid, calcium phosphates and ammonium magnesium (triple) phosphates are usually mixed. They are chalky; the more triple phosphates they contain, the more brittle they become. They are formed in alkaline, decomposed urine. They often cover uric acid, or oxalic acid stones (fig. 736, page 1411). More rarely, they are pure.

The Rarer Stones.—4. **Cystin stones,** are usually rounded, white or sulphur yellow, smooth, with leaf-like fracture surfaces; they may occur in large numbers in the pelvis. Their composition, built up from six sided plates, may be seen in splinters, or better, after recrystallization from an ammonia solution, or even in urinary sediment. They are formed when cystin is excreted through the kidneys, a rare occurrence, and according to Baumann and v. Udransky, Brieger, produced by a decomposition of albumen by particular bacteria in the intestines. Cystin contains nitrogen and sulphur. A cystinuria in which cystin is excreted partly in solution and partly crystalline, occurs in many individuals throughout their life which may be quite long; they have no symptoms until stones develop. As known for a long time, cystinuria occurs in certain families and is hereditary. Abderhalden saw it in three generations of a family living at Basle, and the author had the opportunity of doing an autopsy on a child 21 months old from this family, who had died from a progressive atrophy. In this case of cystin diathesis, the findings were unique: chalky deposits of cystin in various internal organs such as the kidneys, wall of the intestines, mesenteric nodes, liver and particularly massively in the spleen which also contained large amounts of iron-containing pigment. The case was reported by the author and Abderhalden. See also Ackermann, Kretschmer (lit.), Jacoby. Pulverized cystin burns with a blue flame and the odor of burning sulphur or fat.

5. **Calcium carbonate** stones are usually small, white or brown with an earthy fracture surface.

6. **Xanthin stones** are very rare, brittle, flat, glistening, laminated, yellow-brown, or cinnamon-red to dark-brown; the fracture surface, after rubbing, becomes waxy. (Murexid test with ammonia gives a yellow color, and an orange color with liquor potassae.)

The so-called albumen stones (fibrin concretions, or fibrous stones), are very rare; their concentric form occurs through repeated precipitation of colloids, and merely the nucleus may be encrusted, (Lichtwitz, also page 987). Loose tags coming from the surface of the stone may be excreted in the urine as a membranous structure (Morawitz and Adrian, lit.). Most albumen stones give the amyloid reaction (M. B. Schmidt, Miyauchi). Bacteria stones (page 1411) are composed of clumps of bacteria in an albuminous scaffolding; according to Bornemann (lit.), they begin as fibrin stones in which the fibrin is substituted by bacteria (see also C. Meyer and Herzog). The so-called fatty stones are still more rare; they are formed by the deposit of fat from the urine (in lipuria, chyluria) on an organic framework (Schahl, lit.).

See Pfister, lit., concerning indigo crystals in the kidneys, rarely in bladder stones, by which even macroscopically blue stones are formed.

Primary and Secondary Stone Formation.—Ultzmann differentiates "primary stone formation" in which the nucleus is composed of stone-forming substances precipitated in acid urine, and "secondary stone formation" in which the stone contains as a nucleus a foreign body or a sediment from the acid urine. (1, 2, 4 and 6 are primary stone formers, 3 is secondary.) If the primary stone formation with the help of bacteria produces suppuration and alkaline decomposition, there may, as stated above, be deposited thick layers of secondary stone-forming substances (fig. 750 on page 1441). Kleinschmidt speaks of (*a*) diathesis stones (1, pure uric acid stone, 2, 4 and 6) which come from substances which may be excreted in large amounts through the kidneys without changes in the structure of the latter, the amounts so large that there is over-saturation of the urine (see also page 1411); Lichtwitz, however, denies this possibility, since almost every urine is over-saturated with stone forming substances. An increase of this over-saturation, or a disturbance in the colloid equilibrium is said to determine sedimentation (see below). Another type is the inflammatory stone which follows bacterial inflammation and the precipitation of substances set free by these organisms (ammonium urates, calcium oxalate, calcium carbonate, and phosphates); in this case there are, of course, inflammatory changes in the kidneys. The colon bacillus plays an important role in the formation of inflammatory stones, for it decomposes urea (see Munnich, Barth, Cyranka).

Sediments, Primary and Secondary Stone Formation.—According to the colloid chemical viewpoint, the colloids in the urine are in the form of a very dilute sol which prevents sedimentation, *i.e.*, they are protective and keep those substances from precipitating which otherwise are so inclined. When the "protective colloids" are removed from the urine, there remains an over-saturated solution; thus any changes in the colloids, such as coagulation, lead to precipitation of stone-forming material. If sedimentation does occur in the urinary passages, the crystals (similar to those in the urine), and amorphous masses may be stuck together by the coagulated urinary colloids and be intimately mixed in this structureless scaffolding. According to Lichtwitz, the primary factor in stone formation is a coalescence of small, soft sediments which becomes of importance because it provides nuclei for actual stones. Secondary stone formation is therefore a process built around a nucleus; the stone has a laminated structure but the most important factor is the surfaces foreign to the urine; compare page 1411.

The most important consequences of kidney stones are inflammations of the pelvis (calculous pyelitis), as a simple catarrh leading to scarred thickenings, or as a suppuration. The mechanical insults often cause hemorrhages and necrotic diphtheritic changes in the walls, which predispose to perforation. If the ureter is obstructed, there follows hydronephrosis, or pyonephrosis if pyogenic organisms multiply in the stagnating and decomposing urine. Pyelitis of long standing is followed by infiltration of the parenchyma of the kidney by connective tissue or abscesses (pyelonephritis); sooner or later, the entire kidney is destroyed and changed into a thick-walled sac containing stones and pus. In rare instances, the contents are emptied into the abdomen or into the intestines (the latter is spontaneous healing), but more frequently the sac ruptures into the perirenal cellular tissue. The condition which then arises is called peri- or paranephritis (see page 1420), which may take the form of an acute phlegmonous or ichorous process, or when the perforation is slow and there is time for preparation, a chronic fibroplastic infiltration (Hahn).

Occasionally, however, the kidney shrinks to a scarred or fatty structure enclosing the stones. In a 65 year old woman, the author found the left kidney with stones weighing only 27 grams; the hypertrophic right kidney weighed 192 grams. In another 65 year old woman, the left kidney weighed 85 grams, the right 195 grams; in a 56 year old, very corpulent man, the left kidney weighed 50 grams; it was hydronephrotic, and contained a urate stone as large as an almond in the pelvis of the ureter; he had suffered from ureteral colic for ten years, but had been free of symptoms for some time before his death. The compensating, hypertrophied right kidney weighed 265 grams, and a cylindrical stone in the beginning of this ureter had led to severe symptoms the latter part of his life. Death occurred from uremia. In a 48 year old man, the right kidney was removed for extensive tuberculosis; soon after operation, there developed an hemorrhagic enteritis which was found at autopsy to be uremic; there was obstruction of the left ureter by a stone and subsequent pyonephrosis.

If the stone wanders downward, it may produce ulcers in the ureter, which upon healing become strictures. If the stone is obstructed, *e.g.*, where the ureter enters the bladder, there are hemorrhages, ulcerations, pressure necroses and perforations into the abdominal cavity or peritonitis without perforation; it may, however, burrow a way between the ureter and the bladder and thus reach the bladder, as a gall stone may produce a fistula between the common bile duct and the duodenum. The physiological narrow places of the ureter are where the iliac artery and the spermatic artery cross the structure.

Urate stones usually allow x-rays to pass through; they therefore give an uncertain picture. Oxalate stones are quite opaque. Phosphate stones are between these two. Cystin stones are easily detected in a film (lit. by Jacoby). For details of x-ray diagnosis, see Sgalitzer.

When a stone is obstructed in its passage through the ureter, there is stasis of urine above with increased pressure in the pelvis and tubules, with tearing; it is manifested by acute severe pain, the so-called renal colic, which in the beginning, or finally, may be accompanied by vomiting; hematuria is also quite frequent. Quite similar colic may be caused by tumors of the kidney when worm-like blood coagula attempt to pass through the ureter. The ureter itself is said to have no sensory nerves, only sympathetic fibers, whereas its neighborhood is richly supplied; the irritation of the sympathetics, however, through intervention of the spinal cord is projected as pain and tenderness toward the periphery. The pain radiates along the ureter into the bladder, testes and thighs. If both ureters are obstructed (very rare), or if one is obstructed and the other kidney fails because of pathological changes or reflex vasomotor influences, there is anuria; if this continues for some days without removal of the stone, or if the reflex anuria does not disappear, death occurs from uremia. Nephrolithiasis, in addition to the colic, is accompanied by pain in the kidney region and hematuria; the condition can be determined clinically by the demonstration of concrements in the urine. It may, however, run a symptomless course, or be manifested by dull pain in the loins and back, and finally, as in the experience of every pathologist, stones may be found accidentally at autopsy.

See Kumita concerning the experimental changes in the urinary apparatus by stones.

The surgical therapy of renal calculus consists of nephrectomy, nephrotomy, and pyelotomy; the danger from hemorrhage is greater in nephrotomy than in pyelotomy (lit. by Scheyer).

Circulatory Disturbances, Inflammations of the Pelvis and the Ureters, Pyelitis and Ureteritis

Hemorrhages are frequent accompaniments of inflammatory processes, (see below), and certain infectious diseases, especially small pox; in purpura variolosa, the author saw the pelvis and calices stained diffusely dark red. More marked hemorrhages into the pelvis occur in stones, tumors, traumata, animal parasites such as distomum (page 1402), filaria, perforation of echinococci; in such cases cylindrical blood coagula pass through the ureter with colicky symptoms. Inflammations may occur (*a*) from the excretion of infectious substances through the kidneys into the urine (infectious excretory pyelitis, and ureteritis), as in various infectious diseases such as typhoid fever, small pox, diphtheria, pyemia, influenza, (Saathoff and others), also possibly from relatively harmless saprophytes which, *e.g.*, reach the blood from the intestinal tract and are excreted by the kidneys. Such primary inflammations are usually catarrhal, but are often accompanied by small hemorrhages; suppurative inflammation may, however, be added, *e.g.*, in typhoid fever, (Meyer, Ahreiner). (*b*) Many toxic substances such as cantharides, balsam copaiba, etc. produce pyelitis after excretion (toxic excretory pyelitis and ureteritis). (*c*) Autochthonous pyelitis and ureteritis are caused by local conditions such as stones, tumors, parasites (page 1402), blood coagula and true foreign bodies. The most frequent of the forms is calculous pyelitis and ureteritis; the infection is by colon bacilli from the intestines by way of the lymph stream (see Franke); consult the pyelitis of pregnancy, or of women in general, and that of children, page 1364. (*d*) The most frequent form of ureteritis and pyelitis is, however, ascending, from infection of the lower urinary passages or the bladder (ascending ureteritis and pyelitis). Among changes in the urethra may be mentioned gonorrhea, narrowness from strictures, and hypertrophy of the prostate; changes in the bladder include the cystitis of paralysis following diseases of the spinal cord, calculus or tumor cystitis, hypertrophy of the prostate, infection following catheterization, etc. This ascending pyelitis, often followed by suppurative nephritis, usually takes a suppurative or diphtheritic form. Among the organisms found are pyogenic cocci and the gonococcus (very rare, see Bumm), but the most frequent invader is the colon bacillus. Infection may be spread upward through the ureters by continuity from the bladder to the pelvis through the submucous or periureteral lymph channels (Bauereisen), or passively upward in the stagnant urine. The symptoms of pyelitis may simulate those of appendicitis (consult Amann).

The pyelitis, or more correctly pyelocystitis, of childhood is of great practical importance and of frequent occurrence; it prefers female children from 6 months to 1½ years old, and is caused by the ascent of colon bacilli from the urethra. Goppert found them in 1.1% to 1.2% of children learning to talk. The cloudy, light, usually acid, urine contains many leucocytes, casts and a varying amount of albumen. In so-called "defloration pyelitis," there occurs, according to Wildbolz (see also Sippel), an infection with the colon bacillus from the urethra and bladder occurring intra coitum. It is not necessary, therefore, to think of gonorrhea in all acute infections of the urinary tract of the newly married. According to Wildbolz, pyelitis of pregnancy may arise from defloration pyelitis.

The uncommon membranous or pseudomembranous ureteritis may lead to fibrinuria and mucinuria (Senator, Mannaberg, Imbert and others). Discolored scabs appear on the hyperemic, hemorrhagic and ulcerated mucosa and precipitates from the decomposed urine incrustate the mucosa.

If pyogenic organisms become active, an existing hydronephrosis becomes a pyonephrosis. Suppurative inflammations of the kidneys (pyelonephritis) often follow inflammations of the pelvis.

For tuberculosis see pages 1365 to 1373. For peri- and paranephritis see page 1420.

Pyelitis, Ureteritis and Cystic Cystitis.—In chronic inflammations of the pelvis and ureters as well as of the urinary bladder (page 1427), there sometimes appear small miliary, droplet-like cysts which may reach the size of peas (mistaken for tubercles!). They may be thickly scattered and prominent on the mucosa and contain a thin watery, to yellow or thick, sago-like brown content (fig. 738). Opinions are divided concerning their origin. A number of authors stated that they were due to sporozoa (Pisenti, von Kahlden and others), because irregularly shaped homogeneous oval bodies were found in the cyst contents. After considering the peculiarity of the microscopic architecture of the mucosa of the entire urinary tract (Aschoff), the majority of observers have disagreed with this theory. These peculiarities consist of snared-off epithelial masses (v. Limbeck-v. Brunns, epithelial nests), from bridging over of the epithelium of the surface by connective tissue bands, and from budding of the epithelium into the depths (Beneke). Branches and gland-like growths appear, structures found first in adults and with tendencies to separate from the surface of the mucous membrane. Under the influence of chronic inflammation, there is cellular overgrowth, at first, solid and hemispherical or spherical, then cystic, inasmuch as inside of the solid epithelial masses (Stoerk, lit.), there occur hydropic and colloid degenerations, the latter called hyalin (Lubarsch) or mucoid (Aschoff). These produce the sporozoa-like pictures in the cyst contents (see also Stoerk, Herxheimer, Saltykow and particularly the second paper of Stoerk). Perhaps serous transudation (Aschoff, Rona), according to Stoerk, secretion, and perhaps hemorrhages also, (Ribbert) may aid in the cyst formation (see also Segawa). See also pages 1422 and 1436.

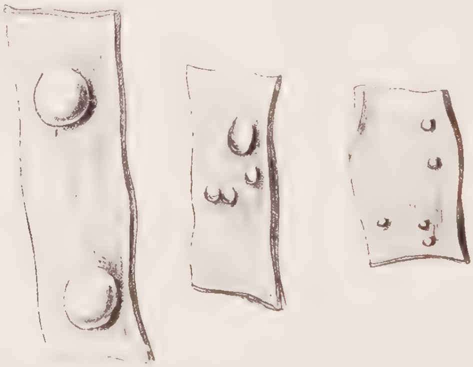


FIG. 738.—Cystic ureteritis; three different portions of the same ureter; nat. size.

Polypoid Pyelitis and Ureteritis.—In chronic pyelitis, usually of the suppurative variety, the mucous membrane may be considerably thickened and show isolated villous, or thick flat polyps. But, in rare instances, polyps occur without previous inflammation. Both of these conditions are quite rare in the ureter. The author performed an autopsy on a young man, who, for years, had excreted rough masses of undigested food in his urine (even pieces of asparagus). There was found a rounded communication as large as a 50 cent piece between the duodenum below the papilla, and the pelvis of the dilated ureter. The kidney itself had undergone such extensive fibrous changes that it could scarcely be recognized in the surrounding fatty tissue. The ureter was dilated sufficiently to allow the passage of a finger, its walls were thickened, and there were many smaller and larger, soft, gray-blue and blue-red polyps, some as long as 2 to 3 centimeters; the ureter had prolapsed a trifle into the bladder and its orifice was surrounded by a rosette of polyps; the posterior urethra was somewhat dilated. Perhaps the course of events was: calculus in the kidney, perinephritis, perforation and emptying of the stone into the intestine.

Epithelial Metaplasia.—The pelvis and the ureter are lined by layers of squamous epithelium, the so-called transitional epithelium. In chronic inflammations, particularly the tuberculous types, the upper layers of epithelium become white and cornified and appear like epiderm (leucoplakia, see Lavonius). Such a dermoid appearance, which some believe to be an embryonal displacement of ectoderm, may also occur in the urinary bladder. If there are mother-of-pearl-like layers of cornified cells and cholesterin plates, *i.e.*, a formed pulp, covering the infiltrated and papillary mucous membrane, the condition may be spoken of as a true cholesteatoma. (lit. concerning cholesteatoma of the urinary passages by Kuttner).

Tumors.—(Spiess, lit. to 1915, and lit. in appendix.) From the mucosa a number of types of carcinoma may arise, such as solid carcinoma simplex, cylindrical cell carcinoma of solid or adeno- or papillary structure, etc. Bauer saw a ciliated adeno-carcinoma. Cornifying squamous epithelial carcinomas occasionally arise in a previous epidermoid metaplasia of the mucosa, *e.g.*, with calculi; in the case illustrated fig. 735, there was a large branched oxalate and calcium stone weighing 93.1 grams in the pelvis. An isolated primary carcinoma of the ureter coming from a papilloma is rare (see O. Chiari, 17 cases in the literature). There are also found occasionally, benign, single or multiple, villous growths similar to those in the bladder (papillary fibroepitheliomas), sometimes with tumors (implantation metastases?) in the lower parts of the urinary passages (lit. by Busse, Savory and Nash, Hryntschak, Blum). Other tumors such as myomas, sarcomas (myxosarcomas, angio-sarcomas, round cell sarcomas), particularly sarcoma-like mixed tumors of lobulated structure, are rare. The author saw a case in a 16 year old woman; see also Fischer and Murakami. Epithelial new growths of the kidneys are often accompanied by stone formation (Stusser, lit.), according to Albarran, in something like 15% of the cases; stones are also held to be etiologically responsible (Blum). Hematuria is often the first symptom. Secondary hydro- or hematonephrosis is frequent (according to Mock in ⅔ of the cases of primary tumors of the pelvis).

For secondary carcinomas see p. 1407; for secondary sarcomas, see *e.g.*, the case in a 30 year old woman with retroperitoneal tumor, p. 873. See p. 1402 for animal parasites of the pelvis. For stone formation, see p. 1409.

Appendix

Perinephritis and Paranephritis. Pararenal Tumors.—Suppuration, involving especially the capsule of the kidneys, or particularly the fatty capsule, is called suppurative perinephritis, whereas further extension into the neighborhood is called suppurative paranephritis. Others call inflammation of the fatty capsule, paranephritis. The inflammation may have a purulent ichorous character.

Origin.—The most frequent cause is suppuration of various kinds in the kidneys and in the pelves. The sac, (fatty connective tissue surrounding the kidneys), may, however, be infected in various other ways; thus as a continuation of an appendiceal abscess, a parametritis, a thrombophlebitis of the spermatic veins, psoas abscess following spondylitis, splenic and liver abscesses, periproctitis, suppurative diseases of the chest cavity, *e.g.*, actinomycosis; furthermore, paranephritis may follow traumatic injury or an operative procedure such as extirpation of the kidney, or tumors, tuberculosis, etc. There is also said to be an independent paranephritic abscess arising from a primary focus elsewhere, such as a furuncle, angina, etc., whereby the suppurative organisms enter the kidneys and from there, without producing local kidney changes, invade the fatty tissue around the kidneys; an independent paranephritic abscess occasionally ruptures through edematous and phlegmonous soft parts into and through the skin.

The rupture of a peri- and paranephritic abscess, or of a kidney abscess, may likewise take place in various directions. The most dangerous ruptures are into the abdominal or pleural cavities. But it may take place into the urinary passages (pelvis or urethra), whereupon pus appears in the urine, into the intestines, particularly the colon, but also the duodenum (see p. 1417 observation of the author), and pus appears in the stools. Rarely, it ruptures into the spleen or the liver, more frequently into the soft parts of the lumbar region and then externally; the abscess may creep along the ileo-psoas region, involve the psoas muscle and burrow downward; there then appear a resistance over Poupart's ligament, and a tumor palpable through the abdominal walls. An external urinary fistula occurs when an abscess, after running a tortuous course, ruptures to the exterior; this presupposes that the paranephritis arose from a suppurative nephritis. Older paranephritic abscesses are surrounded by large amounts of shrinking scar tissue, frequently stained slate-gray, or containing sulphur yellow pus, perhaps calcified. The fatty degenerated pus may also become like chalk.

Pararenal Tumors.—There occur lipomas, lipomyxomas, fibromas and fibromyxomas, sarcomas and sarcomatous mixed tumors (fibro-osteosarcomas), finally, pseudohydronephrotic cyst-like sacs (p. 1405) (lit. by Albarran and Imbert).

URINARY BLADDER

Anatomy.—A large part of the wall of the urinary bladder is composed of smooth muscle in which two longitudinal and one inner circular layer may be differentiated. The outer layer has been called the musculus detrusor; its antagonist is the sphincter of the bladder, a ring-shaped muscular band in the lower part of the bladder immediately above the orfice of the urethra. There is also an internal vesical sphincter belonging to the circular layer, and an external or prostatic sphincter. The muscle fibers display cross bands on the inner surface of the bladder. When the bladder is empty, the anterior and posterior walls almost touch. The epithelium of the mucosa, just as in the pelvis and ureter, is composed of the so-called transitional cells; in general it is composed of several layers; the lowest is not provided with a membrana propria and is composed of low cylindrical cells; then follow round conical, or club-shaped cells in one or two layers, and finally the upper layer of large, often multinucleated, flat cubical cells. Many cells in the upper layers have a half moon or cup-like shape into which the bordering cells of the next layer fit. According to Schridde, the epithelium of the urinary bladder and perhaps of the entire urinary passages is a typical "fibro-epithelium" remaining at a rather low specific level; the formation of highly developed epithelium with kerato-hyalinization and keratin formation as occur under pathological conditions, would therefore be no metaplasia, but a prosoplasia, *i.e.*, a further differentiation (see also Recktenwald).

Small glands, which resemble in structure those in the prostate, and which, like these, contain brown concrements, are found in the urethra just beyond the bladder (Henle). They have been called "aberrant prostatic glands;" they are also found in the female urinary bladder (see

Thorel, lit., Herxheimer, lit.). Otherwise, there are no glands present; those structures which were formerly believed to be glands are gland-like depressions composed of solid epithelial nests (p. 1418). These, and the aberrant prostatic glands, may give rise to cysts. If very numerous, the condition is called cystic cystitis; they are consequences of chronic irritation and occur in a manner similar to those in the ureter (p. 1418). Giani produced them experimentally by irritating the bladder with gelatin capsules and other substances containing tubercle bacilli; the cysts, however, disappeared later, (see the critique of these publications by Stoerk). Lymph nodules in variable number occur in the mucosa, occasionally in the form of prominent plaques or as a diffuse spread.

Malformations of the Urinary Bladder

The urinary bladder develops from that part of the allantoic duct which is hidden in the body cavity, and which in its turn arises from the cloaca, *i.e.*, the last part of the intestinal tract. It is narrowed to a hollow pedicle, the urachus, which continues as the pedicle of the allantois, containing the allantoic duct in its thick mesodermic pedicle; this is also called the "allantois without the bladder." In many animals, the allantois develops as a free-ending blind sac which comes from without the embryo between the vitelline sac and the amion. The allantois of the human does not arise in this manner, but lies as a passageway in the stalk of the allantois, which, by means of the umbilical artery, establishes a connection between the embryo and the chorion, and through this latter with the placenta, and then as the umbilical cord. At the end of the second fetal month (fetus 4 cm. in length), the urinary bladder is a spindle-shaped organ, which empties posteriorly into the sinus urogenitalis, corresponding to the place of entrance of the Wolffian ducts which at the end of the first fetal month are still connected with the ureters, while anteriorly it blends into the narrow urachus, which runs to the navel and then enters the umbilical cord. Toward the end of pregnancy, the urachus, running from the bladder to the navel, is gradually obliterated to become the middle umbilico-vesical ligament; only its lower part remains for a time as an epithelial-lined canal.

If the urachus remains patent at places, there arise urachus cysts; these are usually small, seldom as large as a fist, occasionally multiple, and are found in the median umbilico-vesical ligament properitoneally between the bladder and the umbilicus, usually nearer to the vertex of the bladder. According to Wutz, the epithelium is transitional, consisting of several layers, or is squamous of one layer; the cysts are run through with musculature. (Lit. by Hartmann, Kohlfahl.) See Pendl concerning colloid carcinoma in an urachus cyst. If the entire urachus remains patent, *e.g.*, from stasis of urine in later fetal times, there arises a vesico-umbilical fistula and the bladder is emptied in part through the umbilicus. See Michin, Khaum, concerning primary carcinoma of the urachus which may rupture or extend into the bladder. [For tumors of the urachus in general, see Rankin, F. W. and Parker, B., Surg. Gyn. and Obst. 42: 19: 1926.—*Translator*.]

Excessive dilatation of the fetal bladder may lead to obstruction during labor, (lit. by Michelmann, in whose case the urethra was lacking; and Bohi). At birth, the bladder contains about 3 to 4 cubic centimeters of urine; its capacity is about 10 ccm., but it may contain 100 ccm., (see Broman).

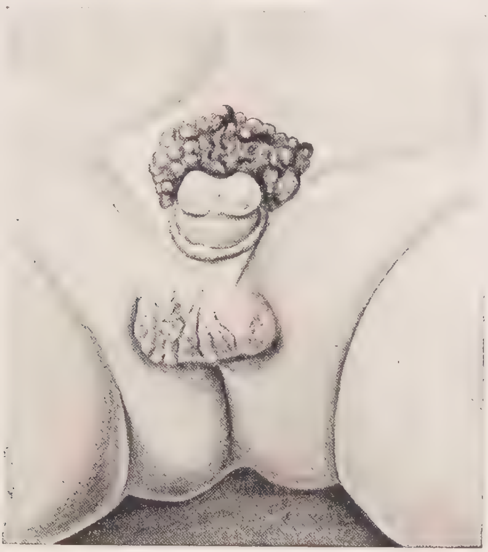


FIG. 739.—Exstrophy of bladder in a child. Above the glans penis (with prepuce) is the markedly nodular bulging everted urinary bladder. The ureteral openings are covered by bulgings. Scrotum on right half is empty and markedly wrinkled. The epispadias is not visible.

The most important defect of development is extrophy of the bladder (lit. by Enderlen), which occurs because of improper closure of the abdominal walls and bladder, *i.e.*, the anterior wall of the bladder is entirely or partly lacking. The bladder, inverted, then appears as a half-round or irregular structure, protruding through the equally open symphysis (fig. 739); the defect in the abdominal wall occasionally reaches up almost to the umbilicus; that which appears to the eye is the dark red folded mucosa of the posterior wall. In the lower part of the hemisphere there can be recognized two protuberances representing the openings of the ureters. The urine trickles from these. The mucosa, often covered with papillomas, blends along its edges with the skin of the abdominal wall. In the ectopic bladder of the newborn, but of children and adults as well, instead of the transitional epithelium, there is squamous epithelium, occasionally in islands, but sometimes covering the largest part, or perhaps a mucus-producing cylindrical epithelium with glandlike structures (Enderlen). Occasionally a prolongation of the skin comes down from the umbilicus across the protrusion and divides it into half. According to Keibel, the embryological explanation of this condition is as follows: if the membrane of the cloaca (p. 722), which at first reaches up to the rim of the umbilicus, is retained too long, *i.e.*, if the body wall is not shoved between the umbilicus and the membrane so that they are separated from one another, and if the membrane is then destroyed, there appears a vesico-abdominal fissure with epispadius (cleft of the penis or the clitoris). Simple epispadius without cleft of the symphysis and higher parts, may be explained by assuming that the process of growth of the abdominal wall stops too early. This growth hindrance theory is based on the work of Reichel, Keibel, Vialleton, Enderlen and others. For a discussion of the various viewpoints, particularly the rupture theory—separation of previously finished parts through hindrance to the urinary outflow—which formerly had many believers, see Enderlen and Kermauner, Hovelacque. In the most severe cases of vesico-abdominal fissure, there is also separation of the pelvic girdle. Cleft pelvis may, however, occur without extrophy of the bladder. An unnatural anus may occasionally empty into the everted bladder. Kuster and others have described intrauterine healing of bladder fissures through the formation of scar tissue, but these descriptions were in error; the cases were most likely an accident to a normal bladder; epithelium may grow over the anterior wall of the bladder from the edges of an abdominal fissure which has adhered to the bladder; this will produce a "scar-like appearance;" or a very small abdominal fissure may heal and the bladder lie behind it (Enderlen).

Carcinomas in extrophy of the bladder (rare, lit. by Enderlen, Lecene and Hovelacque) are mostly adenocarcinomas (Bergenhem); some are colloid carcinomas (Ehrick, Stoerk, and Zuckerkandl, Hager); Wagner saw a keratinizing carcinoma.

If the closed bladder appears in an abdominal or an umbilical fissure, it is a true "ectopia" of the bladder (very rare, lit, by Enderlen), although this term has also been used for inversion of the bladder. The posterior wall of the bladder seldom remains open; if it does, the bladder communicates with the abdominal cavity or with the vagina or with the rectum (cloaca); atresia ani et urethrae may occur coincidently. Bipartate bladder, *i.e.*, complete doubling of the bladder, with at least one ureter in each and their own passageway into the separated or common urethra, and bilocular bladder, *i.e.*, incomplete separation of the bladder into two parts, are very rare and difficult to explain on ordinary embryological grounds (Enderlen, Blum, lit.). The septum producing the separation may run vertically or horizonitally (hour glass form). According to Englisch, they are, in reality, congenital diverticulae (p. 1444), but according to Blum, the congenital hour-glass bladder, the double bladder and the separated bladder are not true congenital diverticulae which are usually found in the neighborhood of the ureteral orifices. Complete absence of the urinary bladder with direct entrance of the ureters into the urethra is very rare (lit. by Pommer).

Circulatory Disturbances

Inflammatory hyperemia is manifested by spotted reddening, particularly along the tops of the trabeculae and folds, while in passive hyperemia, the mucosa is blue-red and the veins are markedly distended; these changes are seen most plainly in the region of the trigone and the neck of the bladder. Marked, usually spindle-shaped dilatation of the veins—the so-called bladder hemorrhoids or bladder varices,—occasionally seen in hypertrophy of the prostate or during pregnancy, may of themselves lead to grave hemorrhage (Vogel), and to difficulty in emptying the bladder. Thrombosis is not rare; the thrombi may undergo calcification. Thrombophlebitis may be followed by a paracystitis and a phlegmonous or diphtheritic cystitis (rare).

Hemorrhages into the tissues of the bladder (suffusions, ecchymoses), or into the cavity, occur in marked hyperemia, particularly in tumors (benign or malignant), in calculous cystitis, after trauma, and very particularly after fractures of the pelvis, in the hemorrhagic diatheses, etc. Larger blood coagulae may change into crumbly brown masses and occasionally become the nuclei of calculi.

Edema of the mucous membrane may be produced by stasis, *e.g.*, in tumors (carcinoma of the uterus and the parametrium), following gynecologic operation with many ligations, inflammatory changes such as severe cystitis, peritonitis, puerperal infection, or trauma, etc.; the mucous membrane is a swollen, puffy, gelatinous mass, or contains vesicles with pedicles (edema bullosum and polyposum). (Stoerk, v. Franque, lit.)

Necrosis occasionally follows pressure of the bladder against the symphysis, or between the symphysis and the skull of the child, from pessaries or forceps, and, as the author has seen together with necrosis of the vagina, from ligation of the uterine arteries in extirpation of the uterus.

Inflammation of the Bladder, Cystitis

Etiology.—The various inflammations of the urinary bladder are caused most frequently by changes in composition of its contents, which, in their turn, are due most frequently to the entrance of bacteria.

Bacteria reach the urinary bladder: (*a*) directly, usually from the use of a catheter sweeping bacteria into the bladder from the urethra, or the catheter itself being infected; after operations of the rectum there is a special predisposition to (hemorrhagic) catheter cystitis (Hadda); (*b*) from the kidneys and ureter; these structures themselves may be diseased and the organisms spread from them to the bladder, or the healthy kidneys may excrete bacteria circulating in the blood, and these then infect the bladder; (*c*) ascending from the urethra, which usually follows primary inflammation of the urethra, particularly gonorrhea, but, spontaneous infection from a normal urethra can occur because, according to Lustgarten and Mannaberg, it often contains considerable numbers of bacteria probably from accidental external origin. This type of cystitis is particularly frequent in women of advanced age, and in children, (colon infection in ascarides, Box), but does occur in men, especially when the opening of the bladder is wide, *i.e.*, the sphincter is relaxed, *e.g.*, in strictures of the urethra, or in diseases of the vertebral column, particularly so-called compression myelitis, when bacteria present in the urethra may be washed back into the bladder in the urine (Rovsing).

Finally a cystitis may arise from extension by continuity of an infection in the neighborhood, *e.g.*, from the female genitalia, from a periproctitis, an infected fracture of the pelvis, etc.

Many irritating substances mixed with the bladder contents, may also lead to cystitis *e.g.*, cantharides, balsam of copaiba and others.

Among the bacteria responsible, there might be mentioned: colon bacilli, and b. proteus vulgaris (Hauser), the latter a decomposition organism; among the specific bacteria are the tubercle bacillus, the ordinary pyogenic cocci and the gonococcus, and, finally, various other organisms which decompose urine (bacterium ureae, micrococcus ureae and others). These latter are termed "ammonia formers" (Leube and Graser); they also produce ammoniacal decomposition of the urine outside of the bladder; under ordinary circumstances they are not pathogenic.

Bacteria may invade the walls and tissues of the bladder, whereupon the urine remains unchanged, but is very acid; in other cases, they decompose the urine and form ammonia compounds which irritate the mucosa. The urine has a very strong odor; microscopically, among other things, the crystals of triple phosphates and calcium phosphate are found.

Many pathogenic organisms both invade the walls of the bladder and decompose the urine. Others, non-pathogenic (bacteria ureae, micrococcus ureae), exert their effect only through decomposition of urea. Thus the staphylococcus and proteus vulgaris may decompose the urine, while the colon bacillus, tubercle bacillus and the gonococcus are not able to accomplish this, so that in these cases the urine remains acid.

Another important factor in the origin of cystitis without invasion by organisms is stagnation of the urine, *e.g.*, in cystocele, and uterine and vaginal prolapse, hypertrophy of the prostate, diverticulae; furthermore, lesions of the mucous membrane of whatever kind, *e.g.*, calculous irritation, are predisposing factors.

These propositions have been demonstrated experimentally by Rovsing. Pathogenic and non-pathogenic organisms are unable to produce cystitis in the normal bladder in animals. If, however, the bladder or the urethra is ligated, or stasis of urine or destruction of mucosa has been produced, infection is easily established.

Anatomic Forms of Cystitis.—In acute catarrhal cystitis, the mucous membrane is spotted and reddened, swollen and desquamated epithelium, pus, mucus and many bacteria are found in the urinary sediment.

In chronic bladder catarrh, the urine becomes muco-purulent, the walls are seriously changed by infiltrations and callous thickenings of the submucosa with overgrowth of the intermuscular connective tissue. The muscle becomes hypertrophic when emptying is made more difficult, or it relaxes and becomes thin when the bladder is paralyzed in spinal diseases etc.; the organ then is very voluminous and easily palpable through the abdominal walls. The mucosa is spotted brown (hemorrhage, pigment changes), covered with muco-pus, shows diffuse or focal thickenings, and papillary or polypoid tumor-like hyperplasias (rare). The loss of the epithelium leaves erosions which may become deep infiltrating ulcers.

Occasionally there are numerous thickened lymph nodules (granular cystitis), or larger prominent plaques, particularly in the neighborhood of the neck of the bladder; swollen nodules may be black gray through the deposition of pigments. Small cysts such as have been described on p. 1418 may occasionally be seen. Epidermization of the urinary bladder is less common; there is, however, reduplication of the epithelium which may undergo cornification and occasionally give rise to cholesteatoma-like, white, pulpy, epithelial masses (p. 1419). The author has seen this condition accompanying calculus cystitis. In contrast to the general opinion that this is metaplasia (Futterer, Lichtenstern, lit.), Pommer (lit.) calls attention to the possibility that it is an embryonal affair, in that the bladder epithelial cells genetically have the power of becoming like epidermis. In pyonephrosis also, the author saw milk-white islands of cornified epithelium, somewhat elevated, in an otherwise unchanged mucous membrane around the trigone.

In the hypertrophic bladder, the seat of chronic inflammation, there are numerous diverticulae, or at least depressions (p. 1445). Chronic catarrh is an accompaniment of calculi and tumors.

Buerger described a chronic callous ulcer (simple bladder ulcer) in chronic catarrh, characterized by superficial precipitation of urinary salts, a necrotic zone, and a layer of young inflammatory connective tissue; the edges are composed of an intensely inflamed mucosa and submucosa. The site of election is around the trigone.

The condition known as "malokoplakia" (v. Hansemann) is usually found with a cystitis, and is characterized by the formation of soft yellow to gray, perhaps red-edged, often numerous, rounded or oval, isolated or confluent plaques from the size of heads of pins to beans. Similar plaques have occasionally been found in the ureters and in the pelvis. Women are more often affected than men. The masses prefer the lower parts of the bladder, and are composed of large cells of peculiar type, of rounded, oval or polygonal form, accompanied in the mucosa and submucosa by such evidences of inflammation as infiltration, and the formation of new vessels in their bases and around their peripheries. The masses usually show surface ulceration and contain bacteria. These large cells are related to Krompecher's macrophages, and contain inclusions (Guttmann and Michaelis) of red and white blood corpuscles, hyalin or colloid droplets, bacteria, and solid hyalin droplets, some in layers, and some, particularly those lying in the depths, containing calcium and iron. But iron and calcium-containing extracellular concrements can also be found (Gierke). Landsteiner and Stoerk call the condition "cystitis en plaques;" they believe these large cells are wandering cells and assume that the condition has a bacterial etiology, in which there are focal infiltrations and deposition of urinary salts (compare Pappenheimer). Hart, on the other hand, believes that infiltration of the walls with urine from the inflamed bladder is the initial damage which leads to the plaques; imbibition on the part of reacting proliferating interstitial cells leads to swelling and to taking up of precipitated inclusions consisting of organic parts, calcium salts and iron coming from destroyed red blood cells. Schmid considers the large cells as wandering phagocytic connective tissue and plasma cells. Minelli feels that this malakoplakia is a non-specific granuloma of unknown origin. Kimla, on the contrary, states that it is related to tuberculosis, (see also Zangemeister), for he found tubercle bacilli in one of his cases (lit. by von Ellenrieder, Schmid, Loele, Waldschmidt, lit., who believe that the etiology has not as yet been discovered; Miche, who disputes its tuberculous nature; see also McDonald and Sewell, who believe the colon bacillus responsible; see also Hedren, Wetzel, Blum, Schmidt).

In suppurative and ichorous cystitis the mucous membrane is covered with pus; many epithelial cells are desquamated. The mucous membrane itself is more or less deeply infiltrated by leucocytes whereupon the process is called interstitial or phlegmonous suppuration. Even the surrounding connective tissue (paracystitis) and the peritoneum may be involved (pericystitis, occasionally, also, general peritonitis).

In cases of longer duration connective tissue growths appear around the masses of pus and as end results there may appear a shrunken or scarred bladder no larger than a chestnut (Ultzmann). An hour-glass shape is due to wide dilatation of the posterior urethra, which is separated from the shrunken true bladder by the internal sphincter (Blum). Perforation of interstitial abscesses may take place into the bladder cavity, *e.g.*, after catheterization (Weigert), since the diseased bladder wall has little resistance. In other cases, younger or older abscesses communicate through small openings with the intestines, the vagina, the peritoneum. The sediment in the urine in suppurative cystitis comprises a thick grayish white mass containing large amounts of pus and mucoid material, the latter the result of mucoid changes in the pus (Kossel), from the action of sodium chloride and ammonium carbonate. The epithelial cells may be so completely destroyed that none can be found in the urinary sediment. This fact is occasionally of diagnostic importance in the differentiation between cystitis and pyelitis, for if the pus comes from above, the urine always contains many epithelial cells, from both the ureters and the bladder.

Multiple metastatic abscesses of the mucosa are very rare. The author has seen them in pyemia; numerous yellow papules the size of the head of a pin were found in the pale mucosa; on section they exuded pus.

In diphtheritic inflammation, also called hemorrhagic necrosis, surface scabs of necrotic and desquamated epithelial cells are mixed with fibrinous pseudomembranes; deep necroses loosen larger masses of hemorrhagic infiltrated mucosa and leave ulcers and thin bladder walls. The necrotic parts appear similar to the membranes in croup. Salts of the alkaline earths are precipitated from the urine, and the parts feel rough. The process usually begins in spots, perhaps as isolated gray or gray white or yellow plaques on the top of the trabeculae, while the depressions between them are still intact. At times, however, a large part, particularly around the trigone, indeed, even the entire inner surface of the bladder, is covered with heavy scabs.

The urine is cloudy, yellow-gray to chocolate in color with large amounts of sediment and a disagreeable odor. Perforation from increasing necrosis usually occurs only when the musculature is paralyzed and thin, and the bladder itself is dilated. Rupture is into the surrounding connective tissue (paracystitis), or, into the peritoneum with fatal results. When the walls are hypertrophied, there are often a phlegmonous peri- and paracystitis. Death occurs with the fever and chills of intoxication, or from pyelonephritis and subsequent uremia. Peritonitis, however, may also develop from direct extension without gross perforation.

Origin: these severe degrees with hemorrhage and necrosis most frequently occur in paralysis of the bladder following spinal diseases, and in urethral stenosis, as from hypertrophy of the prostate or stricture. The ammoniacal decomposition of the urine is the immediate cause. Catheterization may initiate the process. But it may also originate, particularly in women, through extension from the neighborhood, *e.g.*, from a puerperal parametritis, or perforation of an ichorous uterine carcinoma, etc. In still other cases, they develop during the course of severe infectious diseases such as scarlet fever, small pox, septicemia, typhoid fever, etc.

A rare form of cystitis is accompanied by the evolution of gas, (emphysematous cystitis); small gas-filled cysts or vesicles as prominent, transparent, more or less numerous structures, originate in lymph vessels, particularly those in the deeper layers of the mucosa and submucosa but the vesicles and spaces may extend to the serosa. The disease is pathogenetically and probably also etiologically similar to pneumotosis intestini (p. 767), and to cystic colpohyperplasia (lit. by Ruppanner); Nowicki (lit.) at first believed that bacterial influences were minor, while in a later publication he modified this opinion. Schonberg (lit.) believes that bacteria of the colon group are responsible. The symptoms are usually those of only a catarrh.

For cystic cystitis, see p. 1418.

Tuberculosis of the Bladder

There may be differentiated: (*a*) mild and (*b*) severe forms.

(*a*) In the former, the distinct isolated tubercles are surrounded by a red margin; these may become flat, lenticular ulcers with pale bases and mildly infiltrated edges similar to the ulcers occurring in other mucous membranes; they are usually not large and are few in number; occasionally there is but one isolated individual ulcer. Their most frequent sites are in the fundus, the neck and the region of the ureteral orifices. In the relatively frequent unilateral tuberculosis of the kidneys, the ureteral papilla of the diseased side is often recognized by swelling, ectropion and ulceration perhaps extending into the immediate neighborhood.

(*b*) In the severe forms, caseation is rapid and the tubercles, many as large as lentils, soon soften; the confluence of neighboring infiltrations produces deep ulcers as large as half dollars, with caseous bases and caseous undermined edges. These ulcers occur particularly in the places mentioned under (*a*), but often with added well disseminated nodules in the urethra. In the most severe cases, the bladder is markedly dilated, always contains decomposed purulent urine and may still show a few discolored mucous membrane bridges, or, without gross caseation, the mucosa may be ulcerated in toto; the author has even seen perforation into the abdominal cavity. But the inner surface of the bladder in other cases is thickened by many millimeters and covered by a granular, furrowed, yellow caseous layer or by floating shreds superficially encrusted with triple phosphate crystals. (Similar pictures are sometimes presented by diffusely infiltrating carcinomas and sarcomas; see under tumors.) Distinct individual ulcers can no longer be recognized; the entire inner surface is caseous, but the urethra may still show distinct caseous ulcers, occasionally in large numbers, while the prostatic part of the urethra, just as the bladder, is totally caseous. The ureters and the pelvis are usually symmetrically involved.

Scarring of the inner surface is very rare, but the author has seen it both in the bladder and ureters in the case mentioned on p. 1370, (tuberculous kidney weighing 700 grams). The inner surface of the bladder showed a white scar-like background containing red spots and isolated granular nodules. The prostate was composed of a single cavity, with a granular inner surface (Mangold). In contrast to ordinary scarring, the so-called shrunken bladder of the clinician is quite frequent with the symptoms of ulceration, cramp-like tenesmus and continuous urgency (pollakuria); the capacity of the bladder is reduced to 100 or even 50 ccm.

Coincident findings in mild forms are usually pulmonary and intestinal tuberculosis; the bladder tuberculosis is accidental; grave and severe cases are found, as a rule, in conjunction with urogenital tuberculosis, particularly of the male sex organs, while the most severe cases occur in conjunction with tuberculosis of the entire urogenital apparatus.

In many cases, it can be determined that one or both seminal vesicles or epididymis or prostate were first diseased, and from these structures an ascending infection occurred through the spermatic cord, prostate, seminal vesicles, and bladder, from the latter to the ureters and the pelvis (see Rovsing); the ascent to the pelvis is believed to take place in the stagnant urine or through the lymph channels in the outer walls of the ureter (Steven; see Bauereisen). (See the experiments of Wildbolz, Sawamura, lit., Bauereisen and pages 1368, 1372.) On the other hand, when one or both kidneys are severely damaged, disseminated tubercles and caseous ulcers can usually be found in the bladder around the ureteral orifices or in the trigone; if the testes, epididymis, vas deferens and the seminal vesicles are free of the disease, the condition must be the result of a descending urogenital tuberculosis; as a rule, however, the prostate is involved.

Fistulous and larger communications are frequent between the tuberculous prostate and the neck of the bladder and into the urethra.

The spread of tuberculosis to the sex organs and the bladder is more frequent in males than in females.

See Cuturi concerning experiments on the mode of spread of tuberculosis from the tubes and rectum into the bladder (direct, and through lymph channels).

Tubercle bacilli can be found in the cloudy and often bloody urine; in uncomplicated cases it is acid since tubercle bacilli cannot decompose urea.

Syphilis of the bladder is met but rarely at autopsy. Ulcers have been described by Virchow and Proksch. Clinical observations tell of non-characteristic ulcers, tumor-like and papillary changes (Ledermann, lit., Posner, Asch, Dreyer, lit., Baye).

Tumors of the Bladder

Primary tumors are not very common; they are much more frequent in men than in women, are quite rare in children and prefer the deeper parts. The most frequent forms are villous; the most frequent of these are the benign so-called papillomas, or better, "papillary fibroepitheliomas," and the malignant papillary or villous carcinomas. Villous sarcomas and myxomas are rarer. From the clinical viewpoint these tumors were formerly called villous polyps or villous carcinomas, terms which are not recommended (fig. 740).

Papillary tumors occur also in the ureters and the pelvis. As Stoerk has described, cystitis (pages 1418, 1422) is found in conjunction with larger papillomas. There are also benign overgrowths of blastomatous type, in which multiple knorls are formed from secondary overgrowth of the tissues of the mucosa; they are often covered through metaplastic changes by epidermis-like skin (Stadler).

Differentiation of Papillary Fibroepitheliomas from Papillary Carcinomas.- Macroscopically, they may be quite similar, particularly when they have broad bases or broad pedicles and when on pouring water over them they show numerous, floating, plainly dendritic villi (see fig. 745-a and b). The ends of the villi are usually swollen and encrusted with urinary salts; occasionally they have a cauliflower-like appearance. The fibroepithelioma is movable with the mucosa; even in fairly early stages, the carcinoma is fixed. The benign papilloma may be lifted in toto from the mucosa; the villous carcinomas grow from out of the mucosa, and the base from which the tumor springs is infiltrated so that on perpendicular section there may occasionally be observed, even macroscopically, the white carcinomatous infiltration of the bladder wall.

Microscopically, the villus of the papillary fibroepithelioma has a stalk consisting of almost nothing but a thin-walled blood vessel with hardly a trace of connective tissue; the papilla may be plump, or slender and cylindrical; the epithelial covering is composed of a variable number

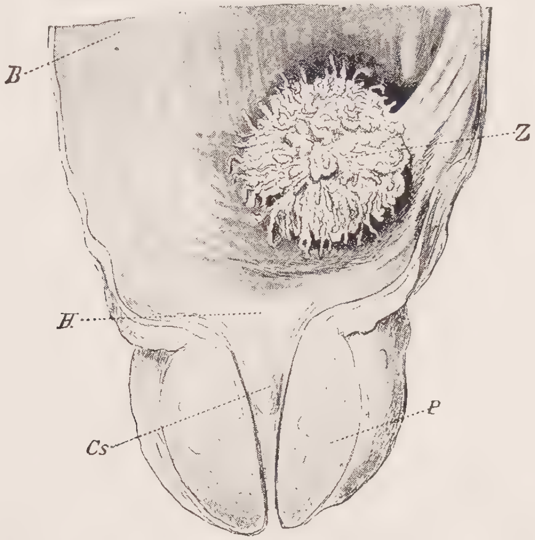


FIG. 740.—Benign villous tumor (Z) (papillary fibroepithelioma) of urinary bladder (B), and hypertrophy of prostate (P). Cs, colliculus seminalis; H, neck of bladder; ⅚ nat. size.

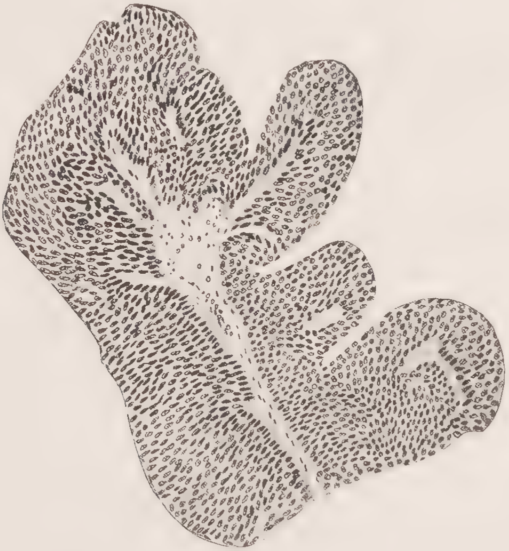


FIG. 741.—Papilla of a "papilloma" of urinary bladder, man 48 years old, which proved to be carcinomatous in its base (fig. 741). The uniformly arranged epithelial covering of the branching growth, similar to bladder epithelium, does not permit the diagnosis carcinoma. (Med. magn.)

of layers, but about the same number as the normal bladder mucosa (p. 1421). The cells are of fairly uniform size and seem to be in a condition of "rest," inasmuch as the cells or the rows of cells are regular and symmetrical and attached practically at right angles to the poorly cellular stalk. The villi in papillary carcinomas are more or less similar to each other, but there is usually much polymorphism of the cells, which are heaped up in thick layers; larger and smaller cells, larger, and often very large nuclei, lie in disorderly masses (fig. 745-c). Occasionally the cylindrical cell polarity cannot be recognized, even among the basal cells.

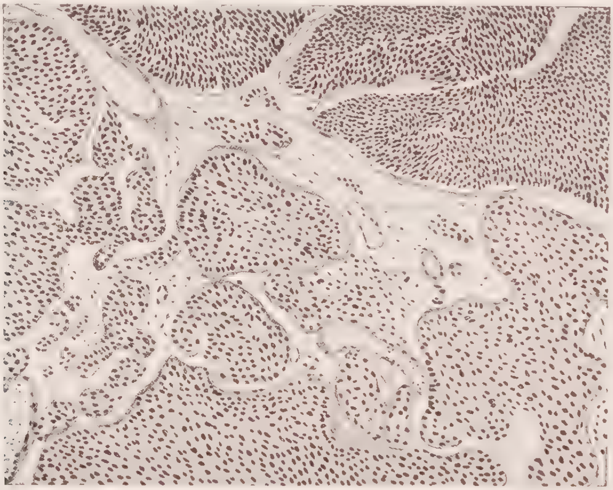
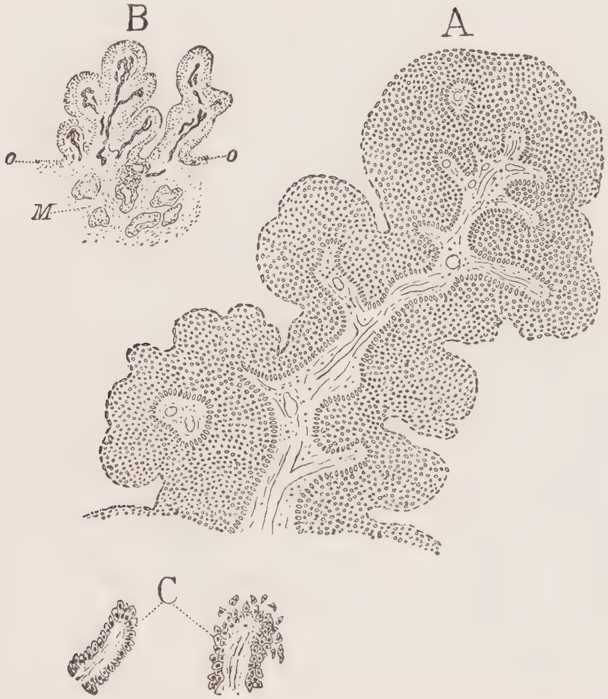


FIG. 742.—Base of the same tumor as fig. 741; the epithelium has become atypical in the depths and forms branching solid plugs which penetrate the mucosa. (Med. magn.)

The most important differentiation, however, lies in the fact that the cells of the papillary carcinoma infiltrate the depths at the point of origin of the stalk (fig. 742), or at least infiltrate into the fibrous stalk of the papilla. Some cells are in solid masses, some are compressed or melted together on a very vascular stalk; hollow epithelial-lined tubes are sometimes produced similar to those of an adenocarcinoma; this calls attention to the fact that the bladder epithelium arises from an anlage similar to that of intestinal epithelium (p. 1424). Epithelial inclusions, the result of horizontal sections, must be properly interpreted; the more certain method can be taken of cutting oblique sections through isolated small villi or systems of villi, so that the invasion and the polymorphism of the cells, with pearls perhaps, are made more apparent. The stalk in carcinoma is often, though not always, well infiltrated by small cells (fig. 742). (See also Zuckerkandl, Syring, Legueu and Verliac.)

It is probable that papillary carcinomas may arise from papillary fibroepitheliomas by atypical growth and invasion; in most cases, however, the carcinoma arises *de novo*. Benign papillomas in both the bladder and urethra may be additions to a villous carcinoma. Both papillomas and carcinomas prefer the lower parts of the bladder (trigone, region of the ureters, region of the internal orifice), and may have multiple primary points of origin. They are more frequent in the later decades of both sexes. If floating parts are forced into the neck through contraction of the bladder, isolated villi may be torn off and expelled in the urine. Hematuria is common, occasionally of such severity that the histologically benign growth becomes suspicious, and not rarely, recurrences appear, often many years after operation in histologically benign tumors.



FIGS. 743–745.—A. Villus from a benign "papilloma" (papill. fibroepithelioma) of bladder. Unusually thick papilla; many layers of epithelium (lowest cells cylindrical, topmost flat, the middle polygonal) cover the vessel-containing fibrous core which is elevated from the bladder mucosa. (Low power.) B. Papillary carcinoma of bladder, diagram. The villi growing upward resemble a benign papilloma, but solid, and gland-like epithelial proliferations grow downward into the musculature of the bladder wall (M); O, normal level of surface epithelium. C. Pieces of delicate villi of a villous carcinoma covered with polymorph. epith. partly detached. (Med. magn.)

The author observed a case (55 year old man), in which the papilloma recurred a number of times during seven years; then a fungoid spindle cell sarcoma arose in another situation, which, after removal in the same year (63 years old), recurred luxuriantly; death occurred in a few month's time (Leuenberger). Papillomas also recur as carcinomas (Hildebrand). These tumors have an outspoken tendency to degeneration; hemorrhage, frequently the first symptom, is often severe, and worm-like coagula appear in the urine; necroses and pulling off of villi are seen; incrustation of the tumor parts with urinary salts is quite common. Perforation of the bladder may follow. There is always an accompanying catarrh of varying degree. They may interfere with the passage of urine and produce a unilateral or bilateral hydronephrosis through obstruction of the ureters.

Other forms of carcinoma are less common. There occur cornifying squamous epithelial carcinomas of soft or scirrhous character, with a tendency to infiltration into the depths and over the surface producing plateau-like thickenings; infiltration into neighboring organs, particularly the rectum, is quite common. Perforation into the peritoneal cavity is followed by peritonitis. Some cases in all probability may be provoked by calculi (see the case described on p. 1437). Squamous epithelial carcinomas without cornification also occur; these infiltrate the entire bladder wall to considerable degrees; only a single ulcer may be present. Such conditions were seen in a 72 year old woman; the bladder was no larger than a small apple; perforation into the vagina took place through a sharply outlined opening; there was infiltration of the iliac and inguinal lymph nodes. A cystitis cystica (p. 1418) may occasionally become a glandular cystitis in which there is a formation of tubes lined by one row of mucous-producing cylindrical epithelial cells; from these there may possibly arise a simple non-villous cylindrical cell carcinoma; mucoid or colloid carcinomas may also have these points of origin (Stoerk and Zuckerkandl, Stoerk, Rauenbusch, lit., Blum, Schmittmann, Weissenbach, lit., Barringer, Pincsohn). Tuberous medullary forms of carcinoma are rare, particularly those forming multiple nodules which undergo decomposition and become encrusted with urinary salts; in such a case the author saw external rupture, invasion of the pelvis, infiltration into the anterior pelvic bones, and softening and liquefaction of the symphysis.

Krompecher has described a carcino-sarcoma, Venulet a tumor appearing like a chorion epithelioma, but, in reality, a carcinoma with metastases in a thirty year old man.

Michin and Schwarz have each described a carcinoma of the urachus situated on the upper pole of the bladder and continuing into its cavity; in Schwarz's case the tumor was as large as a goose egg.

Metastases from villous carcinomas are relatively uncommon; in the infiltrating forms they are more frequent, particularly in the retro-peritoneal nodes, but they have also been seen in other organs (bones, liver, lungs and others).

Bladder carcinomas usually occur in individuals beyond 50 years of age; they are much more common in males; in women they are among the rare tumors. Birch-Hirschfeld has particularly pointed out the latter facts, although others, including the author, have had different experiences (lit. Rauenbusch). According to the records at Basle, in 19 bladder carcinomas (among 1078 carcinomas), 13 occurred in men and 6 in women. All of the 19 with the exception of one occurred past 50 years of age, 12 past 65 years of age; the oldest case was in a man 88 years of age, the youngest in a man 31 years, in whom, 4 years previously, large stones had been removed; the tumor infiltrated the right side and the fundus of the bladder; there were small metastases in the liver. In 22 bladder carcinomas in Gottingen (from 1907 to 1919), 15 occurred in men, 7 in women. Eighteen were in individuals over 50 years of age; the oldest case occurred in a man 93 years old. See Hadda (lit.) concerning bladder carcinoma in youthful individuals.

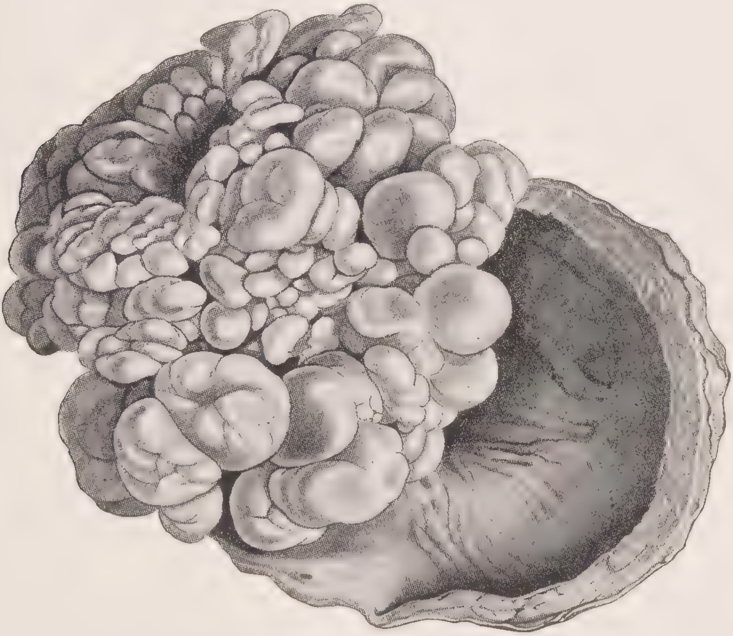


FIG. 746.—Grape-like fibro-myxo-rhabdomyoma of urinary bladder, inserted broadly into the r. side of neck of the bladder. The tumor almost completely filled the bladder and has been lifted out. Trabecular hypertrophy of bladder; boy 7 years old; ¾ nat. size.

Adenomas or **fibroadenomas** (see Thorel) are quite uncommon; they may arise from aberrant prostate glands (p. 1421), from which structures adenocarcinomas and other types of carcinoma may also originate. Some arise from the lower cylindrical cells of the transitional epithelium which line the bladder (see, for example, Ruckert). Bayer described a rare mucoid-forming cyst adenoma. Myxomas, usually multiple, grow rapidly, are transparent, like nasal polyps, and quite rare; they have been seen in children. Fibromyxomas are very rare (Schatz, Albarran, lit.). At Basle, there is a grape-like myxoma as large as an apple, obtained from the right side of the neck of the bladder in a seven year old boy; it had pedunculated vesicular excrescences as large as plums; it was recognized by the author as a fibromyxomatous rhabdomyoma (fig. 746). This type of tumor is very unusual in the bladder; there were found only 3 cases in the literature, 2 in children and 1 in a 22 year old girl; this case is the fourth; (Husler; Monckeberg saw a similar case in a 23 year old girl; see also Sweet, Stumpf). Langhans described a cavernous tumor. Leiomyomas and fibromyomas, occasionally polypoid and as large as a man's head, are very rare (Terrier and Hartmann, lit.). In a 1½ year old boy, the author found a tumor with its pedicle inserted in the trigone; it proved to be an edematous fibroleiomyoma with cartilage inclusions (Husler). These cartilage-containing tumors, as well as the rhabdomyomatous grape-like mixed tumors, which are similar to those of the cervix uteri, may arise from misplaced mesenchyme from the earliest embryonal stages, (Wilms, R. F. Muller, Stumpf).

Rehn, Wendel and Leichtenstern have called attention to the frequent coincidence of inflammations (and granulomas), and true tumors in the bladder, the latter almost exclusively papillomas and carcinomas, rarely sarcomas, in workers in aniline factories. The aniline is said to be taken up through the skin and lungs. The author has seen a number of cases belonging to this category; in one, (59 year old man), there was also a large carcinomatous tumor which filled the pelvis of the left kidney and which infiltrated that organ until nothing but a mere shell remained (compare similar observation of Rehn). In another case, (48 year old man), soft tumor masses almost entirely destroyed the bladder and filled the small pelvis; there were metastases in the lungs. A third case occurred in a 51 year old man in whom a perforation through the fundus into the small intestine had occurred; the fourth case involved a 53 year old man who had worked 25 years in an aniline factory. He also had a shrunken bladder (compare Seyberth). Similar observations from Basle have been published by Leuenberger (lit.). See Lewin, Oppenheimer, Nassauer, Jaffe. For bilharzia carcinomas, see p. 1447.

Sarcomas are rare. Two main forms occur, a tuberous and an infiltrating variety. The former may be nodular, grape-like, or polypoid, covered with villi, and multiple. The infiltrating forms are less common. Sarcomas occur more frequently in women, and relatively often in childhood and puberty.

The author saw a case in a 47 year old woman in whom the entire inner surface of the thick-walled bladder was covered by necrotic tissue masses with floating white or pale gray villi. Microscopically, invasion of the polymorphocellular structure into the blood vessels of the infiltrated wall could be seen. Metastasis occurred to the liver.

Histologically there have been found richly vascular myxosarcomas, round cell or spindle cell sarcomas (see p. 1435) or polymorphocellular sarcomas. The author has also found a lymphosarcoma. In a 15 year old girl, the author saw a grape-like polypoid fibromyxosarcoma as large as a hen's egg in the lower part of the bladder and in the trigone (see Husler). Beneke and W. Fischer have described an osteochondrosarcoma, Ried a chondromyxosarcoma. Leuenberger describes mutation of urinary bladder papillomas into sarcomas. Dermoids, "embryomas," (Wilms), are very rare (Saxer).

(Further literature concerning bladder tumors in the appendix.)

Secondary Tumors.—Carcinomas are quite frequent, coming from the os or the cervix of the uterus, or from the prostate, occasionally from the intestines, chiefly from the rectum. The secondary tumor may grow like a fungus into the lumen of the bladder, or may diffusely infiltrate the wall, or form an ulcer with the development of a fistula; the latter is particularly frequent from the vagina and from the uterus.

In 18 of 27 carcinomas of the prostate, (23 of which were described by the author, Deutsche Chir., Vol. 53, 1902), which occurred in individuals between 65 and 78 years of age, the bladder was involved. The lower posterior part of the bladder is preferred; the most frequent findings are button-like nodules covered by smooth mucosa, or plates, or multiple polyps (v. Hansemann). Some believe that many primary bladder tumors are in reality primary tumors of the prostate which have involved the bladder secondarily (Klebs, Montfori, lit.); the author does not share this belief.

In carcinoma of the os uteri, the author saw such a diffuse, stiff, carcinomatous infiltration of the entire bladder wall that, even though there was no ulceration, incontinence occurred, but such cases are rare. Sarcomas and malignant rhabdomyomas of the vagina, especially the polypoid or grape-like varieties, may grow into the bladder, particularly in small children.

In a 43 year old woman with a carcinoma of the gall bladder and many stenosing metastases in the peritoneum of the intestines, the author saw a secondary carcinoma in the posterior wall of the bladder, as large as a fifty cent piece, nodular and plateau-like.

For so-called implantation carcinoma of the mucosa, see Suzuki.

See under the separate organs concerning edema of the bladder mucosa, particularly in carcinoma of the os and cervix. (Compare also Winter, Kolischer, Zangemeister and others.)

Direct invasion of a sarcoma was seen by the author in the case illustrated, p. 827, of a 48 year old man with melano-sarcomatosis following primary melano-sarcoma of the chorioidea.

Solomin, Lucksch, described local tumor-like amyloid (see p. 323).

Bladder Stones

Bladder stones may be primary in the pelvis of the ureter and wander to the bladder through the ureter, or they may be primary in the bladder. Calculi, composed chiefly of urates, reach the bladder from the pelvis and become surrounded by a covering of secondary calculous-forming substances (earthy phosphates). The same is true of oxalate stones. Bladder calculi are a little more frequent in men of advanced age than in women (about 1%), and are not uncommon in boys.

Statements vary concerning the frequency in various ages, and in various countries (Goebel); this was known to the ancients and was related, probably incorrectly, to wine, and according to recent literature (Abderhalden and Hanslian) to water (calcium content).

Occasionally foreign bodies which usually enter the bladder from without become the nucleus for calculous formations *e.g.*, broken pieces of elastic catheters; in women, hairpins, etc. More rarely, foreign bodies come from structures within, *e.g.*, the contents of dermoid cysts which perforate into the bladder (see under ovaries), and animal parasites (p. 1447). According to their size, they may be differentiated into: sediments (cloudy sediment), urinary sand, urinary gravel, urinary stones. Urinary stones are laminated, and in the larger examples the layers vary in their composition. (Lit. by Finsterer, Kukula.) See p. 856 concerning the important role of distomum nematobium in the pathogenesis of bladder stones. According to Pfister, ovum-containing gravel is formed in the lower parts of the ureter and in the bladder.

A few words will be said concerning calculi in addition to the statements made (p. 1410). (For chemical reactions, see under kidney stones.)

Urate calculi, pure uric acid stones, are hard, small, yellow, red or brown. Calculi composed of uric acid salts are often covered by layers of calcium oxalate and triple phosphates.

Oxalate stones are mulberry shaped (fig. 748), hard and discolored by embedded blood pigments. They are the hardest calculi.

Phosphate stones are white or gray-white. Calculi composed of calcium phosphate are hard, those of triple phosphates are soft and brittle. Struvit's calculi are quite rare; they are composed of rhomboid crystalline phosphates of ammonia and magnesia (Pommer, lit.).

Carbonate stones, pure white and hard, composed of calcium carbonate, are rare, and usually small.

Cystin stones are soft, waxy, often brownish-yellow, or sulphur-yellow, usually egg-shaped and small (p. 1412).

Xanthin stones are cinnabar-red, smooth; the fracture surface is earthy. They become as large as pigeon's eggs; they are very rare.

Number of bladder stones: larger stones are usually solitary, while multiple stones (to 500) are small and may be faceted. The size of bladder calculi varies; they may be as large as peas to hen's eggs and larger. The urinary bladder may be almost completely filled. Littlewood states that the largest stone (observed by Milton) weighed 975 grams. Hochenegg described a stone weighing 2500 grams (observed by Pitha).

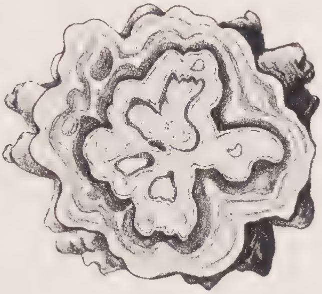


FIG. 747.

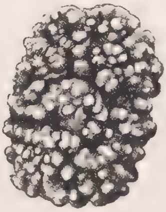


FIG. 748.

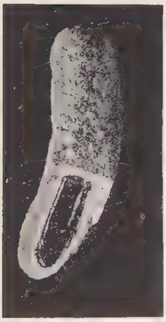


FIG. 749.

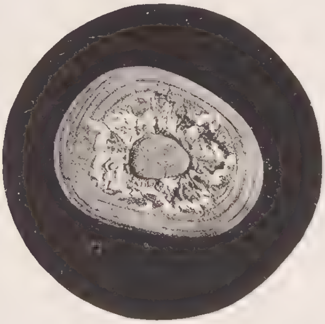


FIG. 750.

FIG. 747-a.—Vesical calculus, beautifully laminated, roughly pronged, crosscut, urate nuclei and oxalate casing; 7/8 nat. size.

FIG. 748-b.—Mulberry-shaped oxalate calculus of urinary bladder; 9½ year old boy; nat. size.

FIG. 749.—Fragment of Nelaton, or Jacques catheter as nucleus of a vesical calculus; ¾ nat. size; man 61 years old with hypertrophy of prostate, removed by suprapubic op. (See Deutsch med. Wochenschr. 1893, 21.) According to the history, the calculus is 3 years old.

FIG. 750.—Laminated vesical calculus; phosphate layers around a small urate calculus as nucleus; man 70 years old, who underwent 4 operations for calculi (once lithotripsy, 3 times suprapubic) removed by suprapubic op.

The contour is mostly elongated, rounded, egg-shaped, occasionally cylindrical or pipe-shaped (Englisch); they are nodular, and seldom faceted; if so, they usually come from the pelvis, where rounded stones may also arise; if elongated, they generally come from the ureters. If foreign bodies become the nucleus of a stone, the contour of the latter may correspond, *e.g.*, elongated cylindrical forms around a piece of catheter.

Occasionally, bladder calculi are found in dilatations of the bladder wall (p. 1444). Spontaneous fracture of these stones is interesting; among various theories, that elaborated by Kapsammer from the ideas of Civiale, is the most popular, that fractures occur through contractions of the bladder, but Englisch (lit.) believes that the solution of substances which radiate from a softened nucleus to the surface in rows and depressions is the principle reason for mechanical destruction.

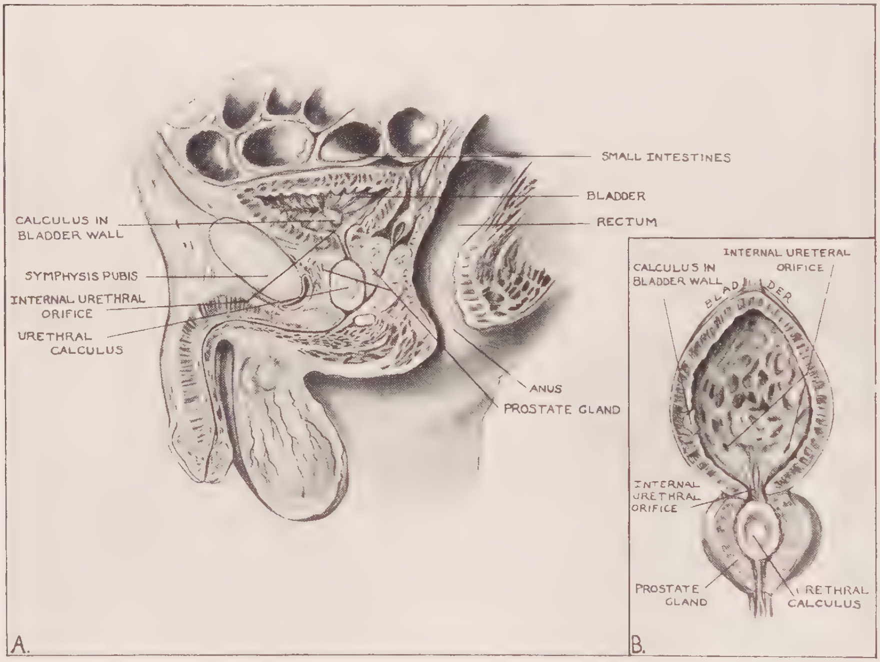

SMALL INTESTINES
BLADDER
RECTUM
CALCULUS IN BLADDER WALL
SYMPHYSIS PUBIS
INTERNAL URETHRAL ORIFICE
URETHRAL CALCULUS
ANUS
PROSTATE GLAND
A.
INTERNAL URETERAL ORIFICE
CALCULUS IN BLADDER WALL
BLADDER
INTERNAL URETHRAL ORIFICE
PROSTATE GLAND
RETHRAL CALCULUS
B.

Fig. 751.—Median section through male pelvis showing the position of a calculus in the urethra. (B) Bladder opened from in front to show the calculus. This patient was 50 years old and died of ascending infection and hydronephrosis. The calculus in the urethra is in the ideal position to produce obstruction, hypertrophy and trabeculation of the bladder. The hydronephrosis and secondary infection of the kidneys are readily understandable from this event. The case is unusual, most calculi being free within the cavity of the bladder. L. H. #173.

The Consequences of Bladder Stones.—There is usually an inflammation of the bladder (calculous cystitis), with frequent hemorrhages (hematuria). When a stone covers the urethral opening, it hinders or completely obstructs the outflow of urine to the accompaniment of more or less severe pain. Frequency and urgency are common. Hypertrophy of the musculature follows long continued vigorous contractions, and finally there is dilatation of the bladder. Pyelonephritis may follow a catheter cystitis. See p. 1428 concerning leukoplacia of the bladder. The chronic irritation of calculi may, in all probability, provoke the formation of a carcinoma (compare the observation of the author on p. 1437, 31 year old man; and p. 1419).

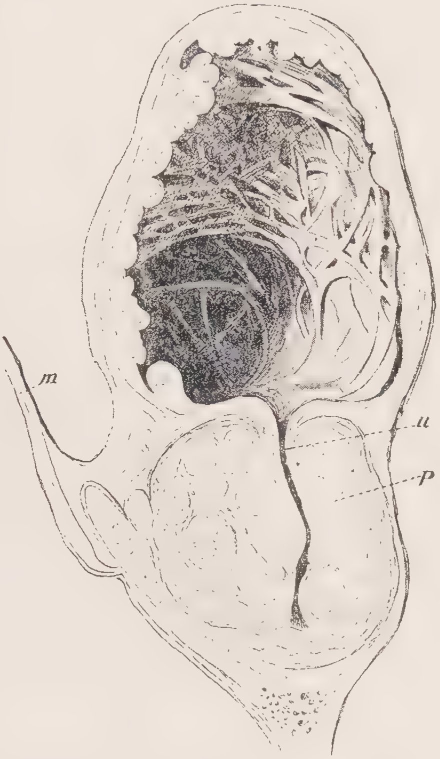


Fig. 752.—Trabecular hypertrophy of bladder with marked, chiefly glandular, hypertrophy of prostate (p); curved course of the prostatic urethra (u); m, anterior wall of rectum; man 83 years old, with pyelonephritis. Sagittal section through specimen hardened in chromic acid; left half; ⅔ nat. size.

Hypertrophy of the Bladder Musculature. (Trabeculated Bladder)

When the musculature is hypertrophied the wall is thick and the capacity of the bladder may be as before (concentric), or increased (eccentric hypertrophy). Marked hypertrophy can be recognized externally by a wrinkled, uneven appearance. Internally the hypertrophic muscle trabeculae appear as criss-cross bands with deep depressions between (trabeculated bladder, fig. 752). As long as the musculature is healthy it is elastic and firm; when degeneration ensues, it softens.

Causes.—(*a*) Obstruction to the outflow of urine from hypertrophy of the prostate, strictures of the urethra, stones, tumors, pressure of a prolapsed uterus, etc. This hypertrophy, often eccentric or characteristic, is a work hypertrophy *i.e.*, it is caused by labor. (*b*) Irritations leading to increased contractions without urinary obstruction occur in chronic inflammations, stones, tumors, foreign bodies, etc.

Dilatation of the Urinary Bladder

General dilatation occurs from stasis of urine, which may be caused (*a*) by obstruction or narrowing of the neck of the bladder or the urethra; (*b*) by paralysis of the bladder. In rapidly occurring dilatation, the wall is almost transparent; if emptying is merely hindered, the wall is hypertrophied.

Partial Dilatations, Diverticulae. Englisch differentiates pockets, or true actual diverticulae, protrusions, the walls of which consist of mucosa and both layers of muscle; and cells, protrusions of the mucosa between bundles of muscles in trabeculated hypertrophy (false diverticulae), designations which are quite useful in many ways (p. 1445).

The pockets (diverticulae) may be larger than the actual bladder, so that the latter appears to be an appendix of the diverticulum. Such structures have been termed erroneously, compartment or separated bladders, or double bladders (lit. by Pagenstecher, Handl). Occasionally a number of diverticulae are present. The walls of diverticulae even though hypertrophied are, however, always thinner and less elastic than those of the bladder because of stretching during micturition. The neck of the bladder, normally narrow when the detrusor contracts, is often very narrow. The diverticulum (giant diverticulum) may contain over 1½ liters (fig. 754); de Quervain records such a diverticulum discovered during removal of a shrunken prostate. Sites of election are the lateral walls, in front of the opening of the ureters (more frequently the left), the base of the bladder above the interureteral ligaments, and the parietal parts related to the bladder end of the urachus. Causes: they may be con-

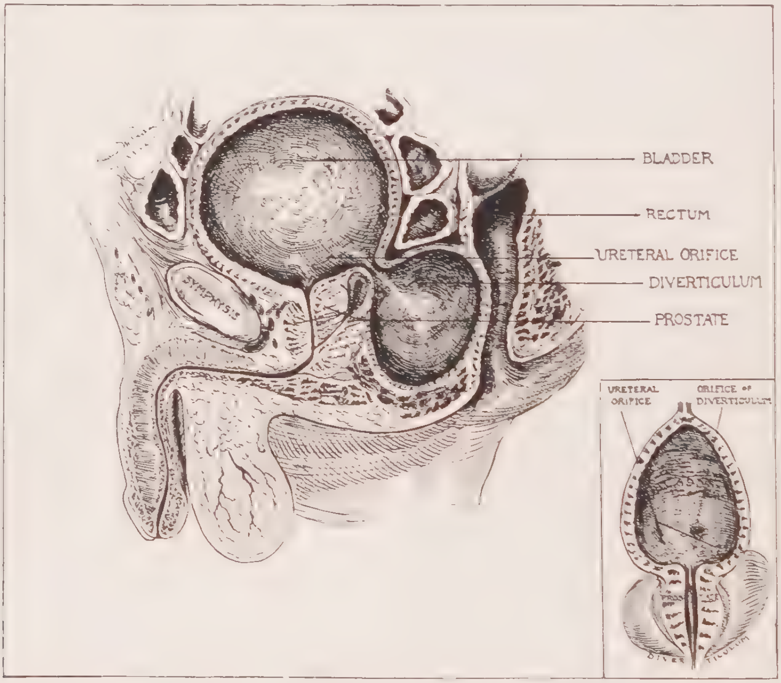


FIG. 753.—Diverticulum of the bladder in a patient 42 years old. Symptoms were present for 10 years. L. H.

genital from failure or hindrance of development (lit. by F. Meyer, v. Hofmann, Brongersma, Blum), or acquired from increase of internal pressure, particularly at places predisposed, by inflammations or fibrous changes in old age (Sugimura); occasionally they may develop from traction from the exterior. Concerning their doubtful relationship to the primary ureters, see p. 1297.

The marked muscle hypertrophy in a bladder containing a diverticulum is at least partly due to a functional overload, since the diverticulum immediately fills up the bladder after the latter has ceased contracting.

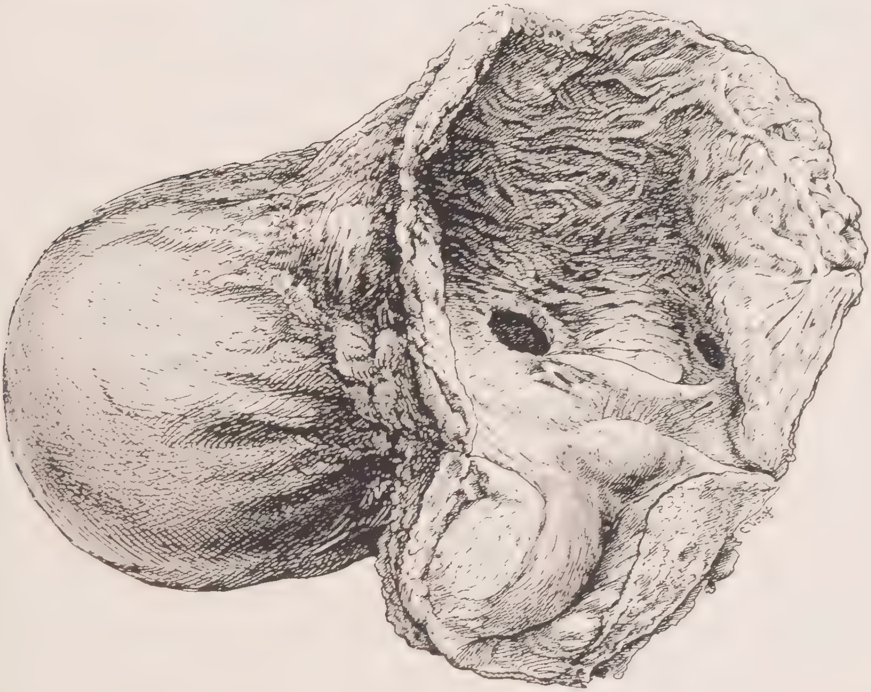


FIG. 754.—Large diverticulum of a trabeculated bladder in hypertrophy of prostate. The diverticulum, relatively thin-walled, with its neck over the opening of r. ureter, contained 1.5 liters fluid; now folded and collapsed. Above the opening of l. ureter, the mouth or neck of a second diverticulum as large as a hen's egg, not visible in illustr.; farmer 77 years old; death from hypostatic pneumonia. Clinically, the diverticulum was supposed to be an echinococcus cyst of liver; ½ nat. size.

The cells, rounded, elongated or mushroom-shaped, are as large as peas to fists, usually multiple, rarely up to 20 or more in number. Their points of origin are above the entrance of the ureters on the posterior and lateral walls of the bladder (fig. 752). Causes: obstruction to the outflow of urine and the consequent increase of bladder pressure, particularly in hypertrophy of the prostate, for in this condition a trabeculated bladder is the usual finding.

Consequences are inflammations in the pockets and cells, pericystitis, adhesions to surrounding tissues, perforation into the abdominal cavity or into the pelvic connective tissue, phlegmons of the prevesical space or of the entire pelvic connective tissue (lit. by Wagner). For entrance into an inguinal hernia, see p. 729. Stones are usually single in the pockets, but in the cells are often multiple. Tumors may also arise in diverticulae. See Eug. Fraenkel for the rarer carcinomas in diverticulae; Leuenberger described a sarcomatous papilloma in a diverticulum.

False diverticuli are abscess cavities communicating with the bladder (Blum), as observed following pericystic phlegmons, etc.

Changes in Position

The most frequent is a vaginal cystocele, a prolapse in which the base of the bladder is pushed toward the vagina; this usually occurs secondarily to the pull of a prolapsed uterus (fig. 822), or retroflexion and retroversion of that organ. Cystocele frequently causes stasis of urine, compression of the ureters and consequent hydronephrosis (Hirokawa); chronic catarrh is the rule. Its presence in hernias, (inguinal, crural, and others), is only partial as a rule, with a diverticulum-like protrusion accompanying a loop of intestine or portion of omentum; these rare bladder hernias occur in older men with hypertrophy of the prostate, as well as in women (lit. by Brunner and Eggenberger, Felten, lit., Finsterer).

In women the fundus of the bladder may be turned inside out and finally appear at the external orifice of the urethra. This is called inversion, invagination or prolapse of the urinary bladder.

Solution of Continuity of the Bladder

This may arise from trauma, (lit. by Bartels, Geill and Nordmann, Galaktinow, lit., Finsterer), *e.g.*, secondary to penetration by pointed bone fragments in fractures of the pelvis, particularly of the horizontal ramus of the pubis. The bladder is usually torn along its anterior wall. It may be ruptured by direct localized blunt force (blow, push, runover). Primary rupture usually occurs in the fundus or close by, near to the posterior surface, but occasionally along the lateral wall; the course is sagittal; a filled bladder is easier ruptured. Spontaneous rupture of a healthy bladder from overfilling is, on the whole, rare (it may contain 3½ liters, Frieberg) (see Hosemann, Moser, lit.). Friedberg (lit.) believes that over-filling under the influence of alcohol (bladder paralysis, alcohol intoxication) is of itself an important cause in a non-pathological bladder. Exertion accompanied by marked contraction of the abdominal walls may also bring about rupture.

Perforation occurs (*a*) into the peritoneal cavity and, as a rule, leads to death from uremia (Rost), or (*b*) extraperitoneally followed by infiltration of urine into the pelvic connective tissue, with consequent urine intoxication (uremia, urotoxemia). Invasion of bacteria and decomposition of the urine result in paracystitis, abscesses or gangrene, which may spread into the entire pelvic connective tissue, and finally perforate into surrounding organs. It occasionally reaches the scrotum and inguinal region.

Among other trauma may be mentioned: pressure of the child's head during childbirth or crushing from obstetrical instruments, particularly the forceps, or, more rarely, pressure from a pessary; the anterior vaginal wall and the posterior bladder wall are coincidently crushed, and there appears a vesico-vaginal fistula.

Pathological changes in the wall predispose to spontaneous ruptures (Oehlecker, lit.) as in erosions from calculi or foreign bodies, suppurative cystitis, *e.g.*, following fractures of the vertebrae with paralysis of the bladder, in softened tuberculous infiltrates, in lipomatosis of the bladder wall (Hedren), more commonly in other tumors, in perforating tumors of the neighboring organs, etc. Rupture from overstretching of a partially degenerated wall occurs in isolated instances, particularly with marked inflammation (Huebschmann); it occurs in the trabeculated bladder of an hypertrophied prostate, infrequently in strictures of the urethra, in which there is usually an ascending inflammation of the bladder (Moser, lit.), in the scars of operations, etc. The carcinomatous vesico-vaginal fistula of carcinoma of the cervix is the most frequent pathological perforation; next in order is a recto-vesical fistula. But primary bladder carcinomas also perforate. External fistulae develop from diseases of the prostate (abscesses, tuberculosis) or traumata (stab wounds, shot wounds, etc.), and may lead into the scrotum or perineum.

Animal Parasites

There may be mentioned: 1. filaria sanguinis (p. 210); obstruction of the lymph vessels produces lymph sacs in the bladder, which finally rupture (hematochyluria). 2. Distomum hematobium (p. 856) may lead to stasis and rupture of the veins and to overgrowth of the mucosa (Bilharz), which may be nodular and finely polypoid. Combined with bilharzia cystitis, Goebel (lit.) has described granulation tumors, benign villous polyps, and malignant tumors (50%) such as sarcomas, but more frequently carcinomas, among the latter chiefly cornifying carcinomas (the so-called cancroids); see also Pfister, lit. Calculi, usually primary, contain the ova as nuclei (Griesinger, Goebel, lit., Ebstein). 3. Echinococci reach the bladder from the ureters or from rupture from other situations and are rarities. 4. Occasionally ascarides and oxyuris reach the bladder through fistulae. 5. Trichomona are also accidentally found (p. 857; Marchand, Miura).

Urethra

Anatomy.—(Lit. by v. Ebner and by Eberth.) In the male, the epithelium of the prostatic part of the urethra is like that of the bladder; in the membranous part it is composed of layers, and in the cavernous part it becomes simple cylindrical. From the fossa navicularis onward it is built up in layers, the upper of cornified squamous epithelium; the junctions are illy defined between the various kinds of epithelium. Isolated Littre's glands and isolated tubular glands are found throughout its entire length. The mucosa is rich in blood and lymph vessels. It contains folds surrounding Morgagni's lacunae; a transverse section of the urethra is therefore not a rounded, but a plicated space. In the male urethra, there empty the ejaculatory duct (vas deferens), and the secondary sex glands (prostate and Cowper's glands). The epithelium of the female urethra shows marked individual variations, being composed of layers of squamous epithelium, or of one layer of cylindrical epithelium (lower part) or of transitional epithelium (above). At the opening of the urethra or in its neighborhood, two pin point openings represent the paraurethral ducts, (0.5 to 2 and 3 centimeters long). According to Nagel and Waldeyer, these structures, first described by Skene, are the ducts of larger gland complexes, related to the prostatic structures of the male urethra, (see also Felix), but according to Kocks and others, (contradicted by Dohrn), they are remnants of Gartner's ducts. Testut called the numerous small mucous glands opening on papillae "periurethral glands." Others describe crypts in the surface of the urethral papillae of irregular number and position, hardly ever more than one to five millimeters deep (Bergh).

Malformations

Congenital malformations are as follows: total and partial obliteration, strictures, (lit. Posner, Hock, Lebrun, lit., Heinecke, Riedel, lit.), folds and malformations in the prostatic part (p. 1528), defects (during the formation of the cloaca), divisions, reduplications (Rona), almost always in male urethras, rarely in females (Grubenmann, Fantl, lit.), and accompanied by round or, (more rarely), by double penis; as far as these are accompanied by epispadius with extrophy of the bladder, they were discussed on p. 1424. Those accompanied by fissure of the penis or the clitoris, (epispadia, the fissure above; or hypospadia, the fissure below), will be discussed under malformations of the genital organs. Congenital diverticulae of the male urethra are very rare, and still more so in the female urethra; they may be noticeable during boyhood as a swelling, usually median, on the lower surface of the penis (v. Bokay). F. Suter (lit.) believes they are a persistence of that part of the genital ridge communicating with the urethra (epidermoid covering); Timofeew speaks of dermoids. Denk, (lit., covering 80 cases), believes that those covered by epidermis are acquired, while those of true congenital origin, usually in the anterior part of the pars cavernosa, seldom further back, are covered with many layers of non-cornifying epithelium on connective tissue papillae. There is also an explanation proposed by C. Kaufmann, *i.e.*, from stasis of urine following delayed communication between the portions of the urethra in the penis itself and in the glans. But the development of the urethra from both these parts is no longer recognized; see R. Meyer. Lit. by R. Meyer, Herxheimer, and in the appendix.

Gonorrheal Inflammation of the Urethra

The most important inflammation of the urethra is gonorrhea, a suppurative catarrh produced by the gonococcus. It is frequent in both sexes, runs a mild to very grave course, can be cured, but may be followed by serious consequences.

Gonococci were discovered by Neisser (1879), were first grown in pure culture on human blood serum by E. Bumm (1886), and were injected with positive results. Wertheim found a simple positive method of culture on a mixture of human blood serum with double the quantity of meat peptone-water agar. See later communications concerning anerobic growth by Buschke and Langer, lit. Gonococci are diplococci, separated by a narrow space; the almost opposing surfaces are flattened (biscuit-shape, coffee bean-shape). In the pus they are usually found extracellular when the secretion is small in amount in the beginning stages and in the stage of healing, or in groups inside of cells, particularly polymorphonuclear leucocytes, but also in and upon epithelial cells; these conditions change considerably according to the mode of obtaining the specimen (Lang). Animals are immune to gonorrhea. See Blair M. Martin concerning the differentiation of gonococci, meningococci and the micrococcus catarrhalis.

It is important to remember that bacteria in more or less numbers are found in every urethra and vagina (Pfeiffer), among them rods of varying thickness and length, streptococci, (streptococci giganteus urethrae), and diplococci, somewhat similar to gonococci but Gram positive (Wahl). In the pus from gonorrhea there also occur ordinary pathogenic cocci in addition to gonococci.

Staining methods are quite simple. A drop of pus is spread between two cover glasses, then dried in the air and flamed, followed by the application of a drop of Loeffler's methylene blue solution. After a half minute the stain is washed off with water. The slide is dried and held high over a flame. Then without cover glass or after embedding in Canada balsam they are observed with an oil immersion lens. In preparations made with carbol fuchsin (2 parts water, 1 part weak solution), the gonococci appear larger.

Since gonococci are Gram negative (Roux), this fact in conjunction with their intracellular position makes the differential diagnosis fairly easy. According to Asch and Adler, those coming from chronic cases may occasionally be, or gradually become, Gram positive. The method according to Gram is as follows: saturated aniline-water-gentian violet solution is used to stain cover glass preparations or sections, 1 to 3 minutes; 1 minute in Lugol's iodine-potassium iodide solution (iodine 1, potassium iodide 2, distilled water 300); absolute alcohol until no more blue color is given off. Wash in water. Counter-stain may be vesuvin or fuchsin in watery solution; gonococci are stained brown or red; other organisms and the nuclei of cells are violet.

When the gonococcus invades the urethra, the first sign is a localized inflammation in the anterior urethra, especially in the neighborhood of the fossa navicularis; this involves both the epithelium and the connective tissue beneath. The organisms are then said to spread through the epithelium (Touton, Wertheim), and invade the intercellular spaces. From the mucosa, leucocytes wander between the cells and to the free surface.

Many epithelial cells swell, soften, and desquamate, others are destroyed in situ. The connective tissue is infiltrated by round cells. Further spread in the connective tissue follows the lymph spaces. The gonococci increase in number in the leucocytes as well as free tissue spaces and lymph channels, and Finger, Ghon, and Schlagenhaufer found them in both epithelial and subcutaneous tissue cells.

The secretion of an acutely inflamed mucosa is thick, intensively yellow or green, occasionally mixed with blood.

The hemorrhages in this so-called "rusty gonorrhea" come mostly from the anterior urethra. (More details by Glingar.)

If the process is stopped at this stage as in mild cases, the epithelium soon regenerates.

Chronic gonorrhea (goutte militaire) in the male remains for the longest time in the posterior urethra, and is characterized by a mild desquamating catarrh and inflammatory infiltration of the subepithelial tissues, or by severer changes in the mucosa and the submucous tissues.

The infection is often confined or held in Littre's glands. Not rarely, the otherwise transparent epithelium of the urethra contains opaque milky-white or pearly glistening plaques of cornified squamous cells, under which the mucosa is infiltrated with round cells. Neelsen and Finger believe that this leukoplakia is a metaplasia and hyperplasia of the epithelium. As epithelial masses are desquamated from maceration or destruction, there appear erosions and ulcers. Cicatrization of the ulcers and connective tissue overgrowth and infiltration into the round cell and plasma cell masses (Rost) in the subepithelial, mucous, submucous, and periglandular connective tissue, particularly in the corpus cavernosum urethrae, lead to strictures of the urethra, the consequences of which will be discussed on pages 1456 and forward.

These scarred strictures are of varying length, and are often multiple, consisting of flat surface growths, or deep networks, or annular scars which may be called cylindrical, nodular, or annular. The most frequent site is at the transition of the membranous into the bulbous part; they may, however, occur at other situations in the pendulous part. The scars may contract so markedly that the entire urethra is contorted. Over the scars the epithelium is most always of the cornified squamous type, and according to Cedercreutz, it is possible that these "epithelial metaplasias" in gonorrhea always arise from islands of squamous epithelium which persist from embryonal times. See this author for lit., and the staining methods of Zilliacus, for the macroscopic differentiation of squamous and cylindrical epithelium. But according to Hubner (lit.), the process is not metaplasia of cylindrical epithelium to squamous epithelium, but a growth of primitive anlage of squamous epithelial cells lying in between the layers of cells of the urethra; under these the gonorrheal infiltrates heal with difficulty, and in the course of years there is a growth of shrinking connective tissue, the callous stricture. See, for opposed views, Rost, and lit. by Kuttner. Behind the stricture, there may grow papillomatous excrescences (rare). For illustrations and lit. see Dittel, E. Burckhardt.

As the gonorrhea becomes chronic, the amount of secretion diminishes, is no longer thick and yellow, but more mucoid; even in later new infections, the suppuration, *i.e.*, the reaction of the mucosa to the gonococcus, is decidedly less. The demonstration of gonococci in chronic, or so-called occult gonorrhea may often be quite difficult because of their sparse numbers, but epithelial cells in considerable number are always found. Culture methods may yield results. (For more details, see Czaplewski.) The demonstration of gonococcus-containing mucoid threads in the urine may be important; many polymorphonuclear leucocytes in these threads is a suspicious finding (Matzenauer); the finding of pus cells without gonococci must be interpreted with care (Leven) for many times these filaments are the harmless residues of a previous infection. The question of whether gonorrhea has been healed is of exceeding great practical importance. It is thought that previous gonorrhea of the man is responsible for 50% of sterile marriages (Fehling).

As accompanying changes of a post-gonorrheal nature, there may occur gonococcus-containing cysts of the neck of the bladder and the posterior urethra (urethrocystitis and urethritis chronica cystica, Buerger).

The spread of the gonorrheal process. The acute inflammation in the male may spread by continuity to the bladder and kidneys, but more frequently into the ejaculatory ducts, then into the sex organs, particularly the epididymis and testes, but also to the seminal vesicles, Cowper's glands, and into the prostate, where it may remain after disappearance of the urethral gonorrhea (Neisser, Putzler). Even the paraurethral passages and Tyson's preputial passages or glands (see under penis, p. 1534) may be infected and remain resistant hiding places for the organisms (for more details, see Grosz). In the woman, the process occurs primarily and with equal frequence either in the cervix where it usually halts, or in the urethra, where there is a characteristic acute inflammation; both of these structures are often attacked. The paraurethral passages (p. 1448) may become hiding places. Extension into the bladder is much rarer (lit. by Knorr) than into the cavity of the uterus and gonococci may be demonstrated during menstruation which seems to act as a provocative; they then spread into the tubes and ovaries, but often first into Bartholin's glands. Those parts of the genital tract which are covered by a tender epithelium are particularly prone to infection, whereas those covered by an epidermoid layer, *i.e.*, the vulva and vagina, are less subject, although these parts may be macerated and inflamed from the passage of gonococcus-containing secretion from above; in chronic gonorrhea, the condition is localized to the cervix or urethra, and the epidermoid layers are then not involved, although the prepuce of the clitoris may provide a hiding place for the organisms (Clodi and Schopper). Distant gonorrheal metastases occur from the invasion of veins by gonococci (Wertheim); thus there are seen inflammations of joints (p. 1238), and of tendon sheaths and bursae (see under those structures). Endocarditis is not a rarity; in a 19 year old man the author saw death occur eighteen days after the infecting coitus; fig. 11, p. 34. This may be accompanied by acute hemorrhagic nephritis (Rotky), more rarely by myocarditis, pericarditis, and myelitis (lit. by Kulbs and Schaffer). When gonococci appear in the blood the condition is called gonococcus sepsis (Socin, lit., Huebschmann, Massini). Metastatic iritis, retinitis, chorioiditis with subsequent phthisis bulbi are also frequent (Greeff). Hematogenous skin metastases are rare (Weill, lit.). (See Nobl for lit. concerning metastatic gonorrheal diseases.) Blennorrhoic conjunctivitis, as frequently seen in the newborn following infection from the mother, is the effect of the gonococcus. See under vagina, for gonorrheal vulvo-vaginitis in small children.

Many cases of gonorrhea are accompanied by severe suppuration in the deeper tissues as evidence of mixed infection from the urethra; the tissue destruction caused by the gonococcus is, in general, much less intensive and rapid than that brought about by the ordinary pyogenic organisms. These suppurative processes take the form of the so-called periurethral abscesses, which break into the urethra secondarily and which lie in the submucosa and even in the corpora cavernosa.

Some of these collections of pus are "false abscesses," *i.e.*, gonococcus-containing pus in Littre's glands (Jadassohn), the excretory ducts of which have been obstructed by desquamated epithelium. Similar gonorrheal pseudo-abscesses are observed in the excretory ducts of Bartholin's glands. Others, however, may reach a length of several centimeters and are true suppurations, among which true abscesses in the prostate are relatively common. Vice versa, abscesses of the prostate may penetrate the urethra.

Other Forms of Inflammation of the Urethra

Primary non-gonorrheal urethritis in the male is also worthy of consideration; according to Grosz, Finger and Nobl among others, the colon bacillus is a frequent offender (Adrian, lit.). According to Halberstadter, non-gonorrheal ophthalmic blennorrhea of the suckling, in which occur cell inclusions (chlazmydozoa) similar to those found by Prowazek in trachoma, is quite similar to non-gonorrheal urethritis of the male. Cohn found influenza bacilli; Konigsfeld and Salzmann (lit.) found the diplococcus crassus. Masturbation and even bicycle riding are said to cause chronic inflammations of the urethra (Oberlander and Hubner).

In women, urethritis may follow inflammation in the neighborhood, *e.g.*, puerperal ulcerative processes of the vagina and vulva. It may also appear during the course of infectious diseases such as typhoid fever, scarlet fever and others. Croupous and diphtheritic inflammations appear in traumatic strictures. Chronic inflammations not uncommonly produce polypoid and richly vascular condylomas. The author saw a richly vascular pedunculated fibroepithelioma as large as a grain of corn just behind the external orifice and the posterior wall of the urethra in a 27 year old man who had had gonorrhea some years previously. The so-called "urethral caruncles" which appear in women close to the orifice of the urethra, and project from the surface, are overgrowths of mucous membrane, (for histology of the normal urethra, see Sachs); they take on the character partly of granulomas, and partly of hypervascular, papillary or telangiectatic mucoid polyps; they may reach the thickness of a small finger and a length of several centimeters and prolapse from the urethral orifice. They often contain adenoid tissue (see Lipschutz), and glands, possibly cystic. They provide excellent hiding places for gonococci (Lange, lit.).

Infectious Granulation Tumors

Soft chancres and syphilitic primary lesions are common. The former may spread over wide areas, and in healing leave scarred stenoses. Tertiary syphilis is also met in the urethra in the form of gummas and ulcers (rare), with possible subsequent strictures (lit. Adrian). It is worth remembering that spirochetae pallida have been found in the urethra of males with primary as well as secondary lesions, but more important, in those who were symptomless (latent); infection of the female (spirochetae pallida in the cervix) may occur from these individuals (Friedlander). Tuberculosis is somewhat more common in the prostatic parts; otherwise tubercles and ulcers are rare, except in severe urogenital tuberculosis when they occur focally as well as along the entire course of the urethra; distinct miliary tubercles are often plainly subepithelial. Lupus may spread into the urethra from the vulva in females, and leprosy may spread in the same way.

Tumors

They are quite rare. Benign epithelial growths of a more hyperplastic nature have been described above as papillary and polypoid; very rarely, they are diffuse (Fluss, lit.). There also occur adenomas which become cystic in parts (lit. Puppel). Primary carcinomas have occurred in the form of squamous epitheliomas, especially in the neighborhood of strictures, in periurethral and perineal fistulae or in previously healthy urethras; adeno-carcinomas have also been described, arising, perhaps, from Cowper's glands; they are very rare. The author saw one case; C. Kaufmann described three cases from the literature; see also Bierbaum. The author observed two cases of cornifying squamous epithelioma following strictures in 63 year old and 61 year old men respectively, (P. Preiswerk, lit.). Hollow depressions, fistulae and abscesses may appear in stenosing tumors. Allenbach saw priapism. Carcinomas of the female urethra are less rare; the author examined a squamous cell carcinoma without cornification in a 55 year old woman; it had surrounded the urethral orifice like a ring; a polypoid papillary cylindrical cell carcinoma occurred in a 51 year old woman (lit. Wichmann, E. Burckhardt, Karaki, Puppel, Tanton, v. Engelhardt, lit., Venot and Parcelier). Secondary carcinomas appear by invasion from neighboring parts, thus from the penis, prostate, uterus and vagina. Furthermore, there occur pedunculated fibromas as well as fibromyomas (Ottow); the author saw one as large as a plum stone at the urethral opening of a 35 year old woman; there also occur hemangiomas (lit. Hanser), as vascular polyps; in a 57 year old woman, the author saw an angioma in the urethra as large as a walnut; it was composed of wide capillaries and veins; the dilated urethra admitted a finger. Sarcomas are rare, among them the melanotic variety; a rare specimen in Basle consists of a flat, warty, spindle-cell sarcoma as large as a bean, taken from a 55 year old woman; there also have occurred lymphosarcomas (Kapsammer). The author, in a 57 year old woman, saw a polymorphocellular spindle sarcoma with many giant cells, which occupied the entire urethra as a hard ulcer, and which invaded the lateral wall of the vagina. Cysts, often of considerable size, arise through stasis of secretion in the so-called urethral ducts of the female urethra (p. 1448).

Tilp discusses local tumor-like amyloid of the urethra (p. 1440).

Solutions of Continuity of the Urethra

This may occur through ulceration, wounds, the passage of stones or foreign bodies, direct trauma, such as stab wounds, shot wounds, etc. Indirect force, *e.g.*, in fractures of the pelvis or in falls, tears the outer surroundings of the urethra or the urethra itself, usually in the pars nuda, or even transversely with wide separation of the ends. In females crushes during childbirth from the fetal head or the forceps are not rare; usually there first occur necroses and then perforation. In the so-called fracture of the urethra (injuries to the erect organ through forced coitus, etc.), the urethra with its erectile bodies alone, or with the corpora cavernosa, may be fractured. There also occur fractures of only the corpora cavernosa penis (see Wasiliew).

Solutions of continuity of the urethra are often caused in strictures (p. 1451) by the passage of catheters; false passages are made from the urethra into the neighborhood or alongside of the urethra to end blindly or to re-empty into the urethra or into the bladder. The chief sites of occurrence are in the pars bulbosa, nuda and prostatica. In severe traumatic tears and crushes the clinical course is very grave and as a rule, if the injuries heal, they leave strictures. But healing is often stopped entirely by the infiltration of urine into the surrounding tissues, which is then followed by suppuration or even phlegmon (periurethral abscesses). Illustrations and literature by Dittel and E. Burckhardt.

Periurethral abscesses spread toward the perineum, and rupture through it or into the scrotum or penis or even on the thigh through a number of openings (external urinary fistulae). They may also run parallel to the urethra and rupture into this structure. Following transverse separation in the pars nuda there often develop enormous abscess cavities in the prevesical space, which at autopsy may be mistaken for an opened urinary bladder. Internal urinary fistulae from rupture of periurethral abscesses into the rectum are rare. If the abscesses and fistulae are old, they are surrounded by a cicatrized wall and may be partially lined by epithelium. If they heal during later stages of the injury, strictures often develop. When abscesses from the neighborhood rupture into the urethra, they form a urinary sac which is called false diverticulum.

Consequences of Stricture of the Urethra

The most important changes in the walls leading to stricture of the urethra are those due to gonorrhea and traumatism. Behind a stricture there is dilatation which may spread to the neck of the bladder and thus produce incontinence (ischuria paradoxa). We may differentiate dysuria, difficult painful urination, stranguria, emptying of the bladder by droplets, and ischuria, complete obstruction to urinary outflow. The bladder wall may hypertrophy or dilate. Recently, the author saw a 72 year old man from whose bladder 2½ liters of purulent urine were removed. The dilatation may spread to the ureters and pelvis (hydronephrosis). Through infection and decomposition, there arise cystitis and pyelonephritis. The ulcers described on p. 1451 become deep and lead to urine infiltration of the surroundings with consequent abscess formation and fistulae. For illustrations, see Dittel.

Urethral Stones

There are differentiated (*a*) primary true urethral stones, usually found in the dilated part behind a stricture or in pocket-like depressions (diverticulum stones). They are composed of phosphates (see Kaufmann, Breitner), and exceptionally of urates (Finsterer). (*b*) Secondary urethral stones come from above; they often have nuclei composed of uric acid salts or oxalates, and enlarge in the urethra where they remain for varying lengths of time in the narrow places such as the pars nuda and the fossa navicularis. Their further increase in size takes place chiefly in the direction of the bladder, or in a true or false urethral diverticulum formed by the stones; perhaps also calculi are in a diverticulum already present, as Finsterer believes in the case of the larger diverticulum stones. These stones have different contours, and their number and size are variable. In the elastic membranous parts, they have been known to reach considerable size (hen's eggs and more). Childhood, and the male sex are preferred (ten urethral stones from a 12 year old boy, Gottingen; W. H. Schultze). For urethral stones in bilharzia, see Pfister.

Cowper's glands, which lie behind the bulbus, the ducts of which empty immediately in front of the bulbus in the pars spongiosa of the urethra, may take part in inflammations of the urethra, particularly gonorrhea. Cystic ectasias occur after obliteration of the openings; these may be followed finally by stenosis of the urethra. Carcinomas have been known to arise from these structures; the author has seen such a case, see p. 1454.

CHAPTER IX

THE SEX ORGANS

Malformation of the Sex Organs.—To understand these malformations, it is necessary to have in mind certain facts concerning their embryology.

At a certain time during embryonal development there appears an indifferent anlage of the urogenital system from which there is further development towards the male or female type.

Embryology

The Indifferent Anlage of the Urogenital Organs. Wolffian Ducts and Wolffian Bodies. (Details and illustrations can be found in the work of H. Bayer, Vorl. ub. allg. Geburtshilfe, I. Bd., Heft 1. Entwicklungsgeschichte des Weiblichen Genitalapparates, Strassburg, 1903; see also Felix, Entwicklung der Harn—und Geschlechtsorgane in Handb. der

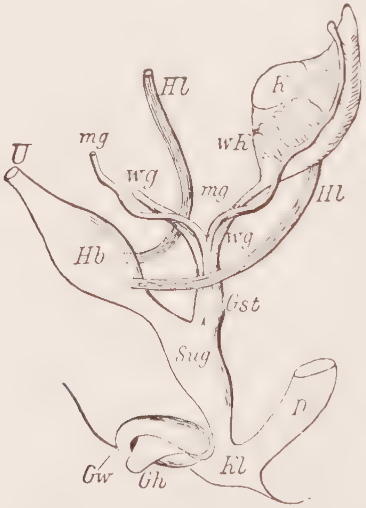


Fig. 755.—Diagram of urogenital organs in early (undifferentiated) stage. After Allen; Thomson from Gertwig, somewhat modified. The parts are viewed from the front; i.e., mg; Muller's duct; w, l. Wolffian body, or l. primitive kidney; k, genital gland (testis or ovary), wg, Wolffian duct; Gst, genital cord, consisting of the two Mullerian ducts and the two Wolffian ducts in one common sheath. The other parts are viewed from the l. side (profile), *i.e.*, U, urachus; Hl, ureter; Hb, urinary bladder; Sug, urogenital sinus; Kl, cloaca; D, rectum; Gh, genital tubercle (penis or clitoris); GW, genital swellings from which the labia majora or the scrotum are formed.

Entwicklungsgeschichte des Menschen, by Keibel and Mall, II Volume, Leipzig 1911, and Broman, Normale and abnorme Entwicklung des Menschen, Wiesbaden 1911. Lit. by Schickele.)

From the fourth to the fifth fetal week, two bodies called the primitive kidneys, the mesonephros, or the Wolffian bodies appear on both sides of the vertebral column. These extend from the anlage of the lungs in the region of what later becomes the diaphragm to the neighborhood of the pelvis. To obtain room for further development, no longer found in the retroperitoneal space, the primitive kidney pushes the wall of the coelom forward in folds into the body cavity. These folds, which later take in Muller's ducts and the sex glands, are called the primitive kidney-sex folds or the plica urogenitalis. The primitive kidney is composed of many convoluted canals coming from pseudo-glomeruli, a secretory part with wide lumena lined by cylindrical epithelium, and collecting tubules lined by cubical, strongly-staining epithelium (concerning hyalin casts, see Rainer), all embedded in a richly cellular mesoderm (embryonal connective tissue). The primitive kidney tubules communicate with the primitive kidney ducts (primary ureters or Wolffian ducts) which become the excretory ducts and empty into the cloaca, the sinus urogenitalis. The secondary or definitive ureters bud from the primary; their openings, however, are pushed more and more in the cranial direction and are thus removed from the primary ureters. The ends of the primary ureters become funnel-shaped and are gradually taken up into the bladder; here they form the trigone between the urethral and ureteral openings, which is pushed in between the actual bladder and the sinus urogenitalis. The epithelium of the trigone is therefore of mesodermal origin, while the bladder epithelium is of entodermal origin (Felix). See page 1292, concerning the relation of the Wolffian ducts to the development of the permanent kidneys (metanephros), and page 1297, concerning their relation to congenital bladder diverticulae at the ureteral orifices. The largest part of the primitive kidney is an embryonal organ and undergoes regression; a part, however, remains and serving the sex apparatus, gives rise to ducts and canals for the passage of specific cell products (ova and semen). [Osborne, Mendel & Terry found a high incidence of phosphatic urinary calculi in rats fed on experimental rations. (J. A. M. A. 69: 32: 1917.—*Translator*.]

In the female, the Wolffian ducts have no permanent significance; in certain animals, rudiments remain as Gartner's ducts, which may occasionally also be seen in humans, even into old age. Compare the remarks on page 1461.

From the lower angle of the Wolffian body there passes a band toward the inguinal canal,—the genito-inguinal ligament—; in the male this becomes the gubernaculum Hunteri which determines the descent of the testes; in the female, it becomes the round and ovarian ligaments. (See R. Meyer concerning this ligament.) It is important to call attention to the fact that the round ligaments which are inserted externally on the tubercle of the pubis, may drag pieces of the Wolffian body along with them in their journey from the primitive kidneys downward (Bluhm, Pick and others); these pieces may be points of origin of glandular-myomatous or cystic new growths.

Germinal Epithelium, Muller's Duct.— The epithelium of the body cavity (coelom epithelium), which in most places becomes flattened to its subsequent peritoneal cells, maintains its early primitive cylindrical form in two places in the primitive kidneys. The first is along a stripe on their lateral surfaces from which later, (later than its neighbor, the Wolffian duct), there arise Muller's ducts, structures which are at first solid strands and which later are canalized; secondly, along a ridge which passes along the medial side of the primitive kidney from anterior to posterior, and into which grows mesenchyme tissue from it. A certain number of epithelial cells develop into genital cells, which through the size of their nuclei and cell bodies may be distinguished from the remaining cells of the body (somatic cells), while the other epithelial cells of the genital ridges retain the primitive appearance of coelom epithelium (fig. 755-k). Germinal epithelium is therefore a mixture of ordinary coelom epithelium and genital cells.

The problem of the primary genital cells, which come direct from segmentation cells is still unsolved, as contrasted with the secondary cells which arise from the epithelial covering of the sex glands; in very young embryos they have been found in the neighborhood of the cloaca, *i.e.*, near the former primitive stripe, and their wandering into the urogenital folds could be demonstrated (Felix). At the time when the indifferent sex glands are laid down, they are found neither extraregionally nor regionally; the primary genital cells therefore disappear. Nor has it been determined whether any relations exist between the primary and secondary genital cells.

The middle parts of the genital ridges become the actual sex glands. The deeper layers of the germinal epithelium are grouped into cylinders and cords more or less sharply separated from each other by sparse mesenchyme tissue. This is the very temporary stage of the indifferent sex glands (first half of the second embryonal month; Broman). Then there occurs differentiation into testes or ovaries with the development of genital cells to spermatozoa or ova, and the development of testicular canals or ovarian follicles.

The Differential Development of the Male and the Female

Male.—(The author follows in part the outline given by Broman.) In the young testicular anlage, the genital cords become sharply separated through a growth of mesenchyme, which wanders in as far as the surface layers of the germinal epithelium and then develops a connective tissue capsule, the tunica albuginea, which is covered by germinal (surface) epithelium. The cords are composed of many small indifferent germinal epithelial cells (supporting or follicle cells), and of larger genital or primitive spermatogenic cells; the masses remain solid up until the end of the fetal time when lumena appear. They are the anlage of the tubuli seminiferi contorti, which later become tubules with many layers of germinal epithelium. At the time of puberty, the genital cells become the spermatogonia, the supporting cells become Sertolini's cells. The genital cords are somewhat branched strands of cells running perpendicular to the surface and converging toward the attached edge of the testes, which become filled out with connective tissue, the so-called mediastinum of the testis. In this mediastinal tissue there lies the rete testis which probably comes from epithelium of the cranial end and which is shortly snared off by surface epithelium; this also is made up of compact cell masses which, however, may be differentiated from the germinal strands through more numerous branchings, smaller strands, darker staining, and smallness of the cells, and particularly by the absence of genital cells. From the rete testis there appear prolongations which are the anlage of the straight tubules of the testes; they meet the genital cords and fuse with them, but remain histologically different. In later stages other prolongations of the rete pass through the mesorchium and unite with the neighboring transverse tubules of the primitive kidney, forming the anlage of the caput epididymis which is enclosed in a tough connective tissue mass; they then unite with these.

The cranially situated transverse tubules of the primitive kidneys usually disappear, but isolated examples may remain and become cysts (pedunculated hydatids) of the caput epididymis. The remaining transverse tubules of the primitive kidney persist throughout life; they, with the parts of the Wolffian ducts belonging to them, are the so-called sexual part of the primitive kidney, and, as stated above, by means of the rete testis, are placed in communication with the tubuli seminiferi contorti. Other transverse tubules which lie caudal to the sexual parts after they have lost their communication with the Wolffian ducts, form the so-called Girald's organ or paradidymis (Ad. Czerny, in animals; according to Switalski, Aschoff and others, also in humans), the situation of which is at the last bifurcation of the spermatic artery before it enters the testis. Primitive kidney glomeruli may persist for long times within this structure. From the caudal transverse primitive kidney ducts which ordinarily disappear quite early, there may remain an aberrant duct of Haller which communicates with the Wolffian duct. Similar aberrant ducts (of the epididymis) may develop from higher situated transverse primitive kidney tubules. The cranial part of the Wolffian duct may undergo atrophy; if it persists, there may appear a cyst of the epididymis. The next part of the Wolffian duct takes part in the formation of the caput epididymis; the tube grows longer and becomes markedly convoluted; the middle and the caudal contortions form the body and tail of the epididymis. Most of the early caudal chief parts of the Wolffian ducts which run in the neighboring urogenital folds, *i.e.*, in the genital cord, become the vasa deferens, (the ejaculatory ducts, the ampulla of the vas deferens and the seminal vesicles).

Muller's ducts, on the other hand, have no significance, and involution begins in the seventh to the eighth embryonal week. Its caudal end remains permanently as a rudimentary atavistic structure, the utriculus masculinus, or vagina masculina, or sinus prostaticus, while from the cranial end there remains the non-pedunculated hydatid of the testis (appendix testis) which is lined by ciliated epithelium and is situated at the cranial pole of the testis. The changes in position which are undergone by the testes, namely, at the sixth month it is in the internal inguinal ring, at the eighth month in the inguinal canal, and at the end of embryonal time it is in the scrotum, were discussed on page 731. This process is known as the descent of the testes.

Female.—For a long time, the ovary has an appearance similar to that of the indifferent sexual gland as described on page 1461. Germinal cords are formed, but they are never sharply separated. The mesenchyme tissue between the cords also grows toward the periphery and is collected into the so-called primary albuginea, which, however, lies deeper than in the testes and is covered by a number of layers of germinal epithelium, the so-called cortical layers; it separates, even though incompletely, the cortical from the medullary layer, which latter is made up of mesenchyme containing embedded germinal strands (medullary strands). The latter, because of its similarity, though slight, to the contorted seminiferous tubules of the testes, is held to be testicular substance; the cortical layer, on the contrary, is the female portion. There occurs, therefore, an hermaphroditic condition; at least, this is the significance placed upon the rete ovarii (compare pages 1542 and 1569), which forms a sort of excretory duct system connected with the medullary strands and with the epoophoron, thus forming an analogue of the rete testis (see Broman). At about the middle of embryonal life, the markedly thickened cortical layer is infiltrated by sparse connective tissue strands which separate the "egg balls" which are larger groups of germinal epithelium, at least, in animals, while in the human there appears an irregular mass of germinal epithelium containing fine connective tissue fibrils (compare page 1541). Since the primary albuginea is splintered, there is no sharp line of demarcation from the seventh embryonal month onward between the cortex and the medulla; later, however, when the follicles have disappeared in the medulla, there is a contrast between the vascular medulla and the secondary cortex which alone contains the follicles. This splintering of the medullary strands and the egg balls goes on until isolated cell groups are formed, which, as a rule, contain only one genital cell, oogonia, primordial ovum (rarely 2 or 3). Such a group is called a primary follicle; the smaller epithelial cells surrounding the primordial ova are called follicle epithelium. The formation of these primary follicles begins during the last embryonal month and extends from the depths of the ovary toward the surface. It is said to cease in the second or third year of life. At birth, the medullary strands have disappeared to small rudiments (page 1569). Secondary, or Graafian follicles begin to appear in the last month of fetal life; for more details, see under ovary, (page 1543). Later, the ovary is pulled by the primitive genito-inguinal strand which remains behind in its growth, and thus descends from above downward, whereby it is placed transversely, one on each side of the uterus (descensus ovariorum). The inguinal band adheres to both sides of the upper end of the uterus and is thus divided into two unequal halves; the longer is the round ligament, the shorter is the ligamentum ovarii. The folds of peritoneum in which the primitive kidneys, ovaries and Muller's ducts are embedded, become the broad ligament.

Both Wolffian ducts as well as both Muller's ducts together form the genital cord and empty into the sinus urogenitalis (fig. 755).

During the course of further development, the primitive kidney remains behind in its growth. (See H. Peters, lit., and Schickele, concerning certain doubtful and certain proved relations of the primitive kidney to pathological conditions; also see under epoophoron cysts, p. 1569, adenomyomas of the uterus, the necks of the tubes, the broad ligaments, cysts of the round ligaments, epithelial, myomatous and cystic tumors of the round ligament as well as epoophoron adenomyomas and those of the posterior fornix of the vagina.) The anterior part of the primitive kidney, (the sexual part), becomes the epoophoron or the parovarium, the analogue of the epididymis in the male, which lies in the broad ligament, and is composed of a longitudinal canal, the remnant of the upper end of the Wolffian duct, as well as of some ten to twenty transversely placed tubules. (For historical remarks concerning this so-called Rosenmuller's organ, see

J. Becker.) The posterior part of the primitive kidney (the primitive kidney part of the Wolffian body) becomes the paroophoron, the analogue of the paradidymis of the male; in the embryo, this structure can be seen for some time as a cellular body, in the adult, as a remnant in the broad ligament often close to the uterus, composed of isolated tubules lined with ciliated epithelium. Of the Wolffian ducts, (in the male, they become the spermatic cords), which lie in the genital cord one on each side of Muller's ducts, there occasionally remain bilateral or unilateral rudiments in the wall of what has now become the genital canal; they are called Gartner's ducts. In many ruminants, in pigs and other animals, remnants are constantly found. In the human, they are frequently found in the lower part of the body of the uterus as narrow canals which send outrunners into the neighborhood of the internal os; in the cervix they are found chiefly in the supravaginal portion near to the cavity and may show marked branching (R. Meyer); after passing into the vagina they turn sharply toward the exterior, to be lost in the upper part of the vagina (Rieder). They are found on one side, or, more frequently, on both sides, even in children (v. Maudach). According to R. Meyer, the epithelium in the principal canal, the ampulla of which lies in the cervix, is usually one layer of cylindrical type, but in the branches and gland-like structures it is small and cubical. See R. Meyer (lit.) concerning congenital abnormalities, cysts, benign and malignant tumors, adenomas and carcinomas of these structures; concerning epithelial new growths in the rectogenital interstitial tissue of the female, see Bumke. The tunica of Gartner's ducts consists of connective tissue and circular musculature. See Schottlander (lit.) concerning malformations of the uterus with persistence of Gartner's ducts.

Muller's ducts are of great importance in the female. The anterior portion becomes the Fallopian tube, the posterior, the uterus and vagina; the so-called hydatid of Morgagni, a small pedunculated vesicle, is connected with the abdominal end of the tube by a small thread. The lower ends of both Muller's ducts fuse; when their dividing wall disappears, a simple tube (genital canal) results. The vagina first becomes a single tube, and then the uterus appears; in the beginning, a paired organ (end of the fourth month), the saddle-shaped concavity in the fundus, which is the last sign of the lateral horns, is lost (end of the fifth month) as the uterus increases in size until the fundus actually becomes convex. The uterus receives a strong musculature, and is separated from the vaginal portion (beginning of the fourth month). The hymen is formed in the fifth month and consists of two layers, the inner coming from the vagina, the outer from the vulva (Schaffer, Taussig).

Development of the External Sex Organs.—It is necessary to go back to an earlier stage of development. Wolffian and Muller's ducts (fig.

755) empty into the sinus urogenitalis; this is the end of the allantois, the upper part of which becomes the urinary bladder and the urachus, while below it enters the cloaca into which the rectum also empties. The urinary and sex passages as well as the intestines therefore empty into the cloaca (more details on p. 722). During the sixth week, before the perineum is formed, and the separation into anus and urogenital openings is brought about (tenth week), there arises in the cranial direction the genital tubercle (1), from the cloaca membrane (see p. 722), while the lateral margins of the cloaca membrane are thrown into folds, the genital folds (3), which form a boundary around the cloacal fissure by forming a ring-shaped prominence (2). On the lower side of the more and more prominent and hook-shaped genital tubercle there arises (end of the second month) the sexual furrow (4), which runs downward to the cloacal fissure. The tubercle becomes larger, and the furrow is deepened by the growth of the genital folds (3). The sexual tubercle appears in the third month as the sexual organ. At the same time, the separation of the rectum and the urogenital openings is accomplished.

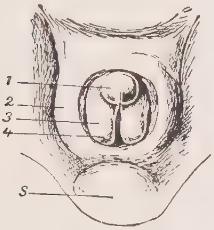


Fig. 756.

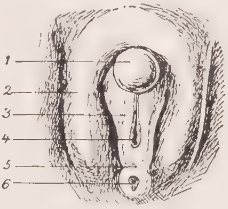


Fig. 757.

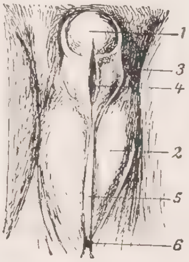


Fig. 758.

Figs. 756–758.—Various stages of development of the external genitalia (after figures in Hertwig, Entwickgesch. 2nd edit. p. 313) which were prepared from wax models by Ecker-Ziegler—freely transposed.

Fig. 756.—Stage in which sexual differentiation is not yet visible; 1, genital tubercle; 2, genital swelling; 3, genital folds; 4, genital cleft; s, caudal end (embryo 8 weeks).

Fig. 757.—Transformation into female type; 1, clitoris; 2, genital swellings become labia majora; 3, genital folds produce nymphae; 4, entrance to urogenital sinus or vestibule of vagina; 5, perineum; 6, anus (embryo 2½ months old).

Fig. 758.—Male type; 1, glans penis with prepuce; 2, scrotum; 3, genital folds which grow in the middle toward 4, genital cleft (urethra); 5, scrotal raphe; 6, anus (3 m. old e.).

The Further Development of the External Sex Organs

Male (fig. 758).—The sexual tubercle rapidly becomes the penis, and even in the third month, there is a suggestion of glans. The sinus urogenitalis becomes the elongated narrow urethra; the furrows on the under surface of the genital tubercle elongate with the enlargement of the latter, and fuse, to a small opening on the glans (fourth month). See Felix, concerning the formation of the prepuce, which grows from the outer surface as a solid and later hollow cylinder of epithelium; for more details, see R.

Meyer. In the posterior part of the urethra at the beginning of the sinus urogenitalis, the prostate appears in the third month as a ring-shaped swelling, containing smooth muscle, in which the epithelium grows in the form of glands. Cowper's glands, and in the woman, Bartholin's glands, also develop by ingrowth of the epithelium of the urethra. The genital folds, which in the female become the labia majora, grow together in the median line (raphe scroti) and form the scrotum, into which, as stated on p. 1462, the testes wander toward the end of embryonal life.

Female (fig. 757).—The changes are much less complex than in the male. The genital eminence develops moderately into the clitoris, which develops a thickening analogous to the glans penis; it is covered by a prepuce from the genital folds. The genital folds, in addition to forming the corpora cavernosa urethrae, develop into the labia minora; the short sinus urogenitalis lying between is called the vestibule; this includes the openings of the urethra and the vagina, the latter of which is formed through the fusion of Muller's ducts. The outer genital folds become the labia majora.

True and False Hermaphroditism.—According to Poll, there may be differentiated: (1) essential or germinal sex characteristics which are brought about through differences in sex cells (gametes), and (2) accidental sex characteristics to which latter belong: (*a*) as genital findings, the genital passages; (*b*) as extragenital findings, the voice, psychic qualities, body form, (growth of hair, color, etc.). But there may also be differentiated (Pick), hermaphroditism as a mixture of the opposite sexual characteristics into true hermaphroditism (androgynia), which is a mixture of essential (gametic) characteristics, and pseudohermaphroditism (spurius), as a mixture of accidental (somatic) sexual characters.

The term "asexual" is used to denote a lack of all sex organs as usually seen in connection with grave malformations of the entire body or with clefts in the lower half of the body (cleft bladder, cloaca formation).

Neutral hermaphroditism consists of entire lack or rudimentary development of the sex glands. Virchow called such individuals, "homines generis neutrius," or "asexuelle nutri;" others are neutral bisexuals with ovotestis (see below) but a functionless testicular part; the external genitalia are usually of the male type (see Uffreduzzi). See also Meixner, Wessel, concerning the determination of the sex in hermaphroditism.

True Hermaphroditism.—Based upon the older differentiation as outlined by Klebs, and with due consideration to later researches, there may be differentiated:

(*a*) **Bilateral** true hermaphroditism; on both sides either a testis and an ovary or an ovotestis (hermaphroditic gland).

(*b*) **Unilateral** true hermaphroditism.

(1) Complete; on one side either a testis and an ovary, or an ovotestis; on the other side one sex gland (testis or ovary). There are eight possible varieties of this condition, and they are spoken of *e.g.*, hermaphroditism verus unilateralis completus masculinus dexter with ovotestis or separated sex glands, when on the left there is either an ovotestis or a testis or a testis and ovary, and on the right side a testis; the condition is spoken of as hermaphroditism verus unilateralis completus femininus dexter, when there is an ovary on the right side, and on the left two separated different sex glands or one ovotestis; etc.

(2) Incomplete; on the one side there is no sex gland, on the other side an ovotestis or a separated testis and ovary. There are four possible varieties, thus hermaphroditism verus unilateralis incompletus dexter and sinister, according to whether an ovotestis or a testis and ovary are on the right or left side.

(*c*) Hermaphroditism verus lateralis s. alternans; on the one side there is a testis, on the other side an ovary. If the testis is on the right or left, it is spoken of as dexter or sinister (Kleinknecht, Photakis, lit.).

Consequently there are eighteen possible variations of hermaphroditism, such as are set forth in the following table:

Scheme of the 18 Possible Variations of True Hermaphroditism

(*a*) True Bilateral Hermaphroditism

Right	Left
1. Testis and ovary	Testis and ovary
2. Ovotestis	Testis and ovary
3. Testis and ovary	Ovotestis
4. Ovotestis	Ovotestis

(*b*) 1. Unilateral Complete True Hermaphroditism

Right	*Left*	
1. Testis	Ovotestis	True hermaphroditism unil. compl. mascul. right
2. Testis	Testis and ovary	True hermaphroditism unil. compl. mascul. right
3. Ovotestis	Testis	True hermaphroditism unil. compl. mascul. left
4. Testis and ovary	Testis	True hermaphroditism unil. compl. mascul. left
5. Ovary	Ovotestis	True hermaphroditism unil. compl. femin. right
6. Ovary	Testis and ovary	True hermaphroditism unil. compl. femin. right
7. Ovotestis	Ovary	True hermaphroditism unil. compl. femin. left
8. Testis and ovary	Ovary	True hermaphroditism unil. compl. femin. left

(*b*) 2. Incomplete Unilateral True Hermaphroditism

1. Ovotestis		True hermaphroditism unil. incomp. right
2. Testis and ovary		True hermaphroditism unil. incomp. right
3.	Ovotestis	True hermaphroditism unil. incomp. left
4.	Testis and ovary	True hermaphroditism unil. incomp. left

(*c*) Lateral or Alternating True Hermaphroditism

1. Ovary	Testis	True hermaphroditism lat. s. alternans left
2. Testis	Ovary	True hermaphroditism lat. s. alternans right

Newer investigations, paying particular attention to the histological conditions, have shown that the existence of a true hermaphroditism cannot be demonstrated in most of the described cases. Thus O. Schultze does not believe that (*a*) and (*b*) have occurred. But he does admit the occurrence of a lateral hermaphroditism, while Nagel, and Kermauner emphasize, that, up to the present, there has been no undoubted case of true hermaphroditism reported, in the sense that the individual had separate testes and ovaries, not even in monsters which have died early. Salen, Garre-Simon, Pick and others, however, have described cases which they believe to be true hermaphroditism, because on one side there was an ovotestis demonstrable as a well defined structure. Kermauner and Sauerbeck believe that only the cases of Salen and Simon are free of doubts (compare Marchand). Recently, the cases of Uffreduzzi, Gudernatsch, Photakis (lit.), Polano (lit.), have been added to this list. However, the sex glands were probably not capable of function in these cases, whereas the functional ability of the glands is the one sure sign of true hermaphroditism. (Cinoare, also Bayer, R. Mayer, Meixner.) But even though in these cases, as well as in true hermaphroditism of mammals, the simultaneous presence of male and female sex cells has not been demonstrated as a rule, they nevertheless agree so well with the case of Salen as reinvestigated by Pick, that the actual occurrence of a true hermaphrodite in the strictest sense of the word has been undoubtedly shown. And even though in the majority of cases there is a lack of the specific cells of both sexes, yet, according to Pick, this is no ground for the belief that they are not sex glands, since they contain the remaining specific structures of these glands. Therefore the finding of testes in which there are no germinal cells is not a proof that they have not been present previously, just as occurs in the otherwise specifically composed testes of cryptorchids. Hermaphroditism and pseudohermaphroditism represent various degrees of departure from the normal, and in their structures are peculiarities of malformations, and not atavistic failures of development. Knowledge of these conditions has been greatly advanced by the studies of true hermaphroditism in lower animals as well as in the pathological malformations in the form of true hermaphroditism in birds and mammals (pigs, calves, goats). (See also Kitt.) [For case of true bilateral hermaphrodism, see Burden, V. G., J. Urol. 12: 153: 1924.—*Translator*.]

Pseudohermaphroditism.– This condition is caused by failure of the anlage and of appearance of the sexual characters; according to the kind of sex glands, which may be very difficult to determine during life, the condition may be divided into pseudohermaphroditism masculinus and femininus, and these in their turn, according to Klebs, into internal, external and complete. External hermaphroditism occurs when only the external genitalia, internal when only the internal organs, and complete when both internal and external organs, are not properly developed. See Thaler concerning familial pseudohermaphroditism in blood relatives.

Male hermaphroditism is much more frequent than female, and most of the outspoken cases are of this type. The complete cases have testes, vasa deferentia and prostate, with development of Muller's ducts into a vagina, uterus and tubes in more or less complete fashion. The external parts are more or less similar to the female type. This is also the case in external pseudohermaphroditism in which the normal internal male genitalia are found, while the much more rare internal type shows, externally, typical male genitalia, in which, however, internally, in addition to normal or rudimentary male sexual passages (epididymis, vas deferens, seminal vesicles, ejaculatory ducts) there are partly developed Muller's ducts which have formed a sort of vagina, uterus and tubes which empty into the urethra in the neighborhood of the colliculus seminalis. The conditions are easily understood from the diagram in fig. 755. The most striking finding is the similarity of the external genitalia to those of the female type. These changes are very easily explained, inasmuch as parts which should have grown together, remain open. Thus the sex organ is insufficiently developed like a clitoris; the rim of the sexual eminence remains open. The sinus urogenitalis is wide open and deep, or the sex folds have not joined to form a scrotum. If the testes do not descend, there is great external similarity to female genitalia. If the retained testes are poorly developed, and if such individuals fail to have other characteristics of the male such as beard, voice, sexual desire, well developed musculature, etc., and if, as usual, if not always, the external habitus follows the external sex parts (female) and not the true sex (testis), it is easily understood that such individuals may pass as women. From this extreme there are variations to cases which merely belong to the hypospadia, in which the under surface of the penis has remained open. In mild degrees the opening of the urethra may be on the under surface of the glans, but the remainder of the organ is entirely normal; in severer cases the organ is short, and thus similar to the female type, particularly when the testes have not descended. A marked hypospadius is a pseudohermaphroditism masculinis externa, pseudothelia. See Moller for illustrations of complete masculine pseudohermaphroditism.

Female pseudohermaphroditism, because of its infrequency (842 male to 128 female, Neugebauer), is of less importance. In external female pseudohermaphroditism, the clitoris may reach the size of a penis; in severe cases the ovaries, which are usually poorly, and rarely completely, developed, may descend into the labia majora and simulate a scrotum; or the opening of the vagina may be narrowed, the labia grow together entirely or in part, and between them the urethra and the vagina open into a small furrow (sinus urogenitalis). In the severest cases, the external orifice of the vagina is entirely lacking; it empties into a urethra surrounded by a prostate, which is elongated into a sort of sex organ with a more or less open channel (hypospadius of varying degrees). Such individuals may pass as males; they may be called "pseudarrhenia" (Benda); their external genitalia are of a fairly complete male type, and the secondary sexual characteristics show a growth of beard, pubic hair in triangular form, male pelvis, lack of breasts, male larynx; otherwise the sex glands and the genital tract are of the female type. Many severe cases have been classified as complete feminine pseudohermaphrodites, especially when there is a prostate developed (Ziegler), but erroneously so, since the prostate in its development belongs to the external, and not to the internal genitalia (Orth, Fibiger, lit.); these are external female pseudohermaphrodites. But perhaps they can be put in a class by themselves, because of the presence of the prostate and because of abnormal development of the adrenals, particularly in the form of enormous hyperplasia (Marchand), with the possible presence of adrenal tumors and inclusions, all of which characterize the malformation in these individuals as a particularly deep one. In fact, these conditions may be looked upon as something peculiar to feminine pseudohermaphroditism (lit. by P. Fraenkel), especially because similar malformations are found only in isolated cases in the masculine type (Brutschy, lit.). In true hermaphroditism, adrenal hyperplasia has never been found, but, according to Brutschy, malformations of the genitals and hyperplasia of the adrenals, nevertheless, are dependent upon each other. See Mathias concerning reversal of the sex characters in the presence of hypernephromas in which the sexuality of these individuals was usually directed toward the female characters, and not rarely, quite vigorously so. An abnormal persistence of the Wolffian ducts belongs to feminine pseudohermaphroditism.

For the new growths in the sex glands of hermaphrodites or pseudohermaphrodites, (dermoids, ovarian cysts, adenomas, carcinomas, sarcomas, teratomas), see L. Pick, Chevassu, the author, Zacharias, Keller, R. Meyer, Schwarz, (lit.), Polano. Lit. concerning hermaphroditism by v. Neugebauer, Kermauner, Sauerbeck, Meixner, Pick (lit.), Mittasch (lit.); see also Christeller.

Malformations of the Female Genital Apparatus (Lit. in Appendix)

The malformations of the female genital organs are easily understood in the light of their embryology. The chief forms are: (1) an incomplete relationship, or an incomplete disappearance of parts which should have been joined; this leads to duplication, and reduplication; (2) rudimentary development (hypoplasia) of parts in which structures which should have been opened, are closed; there arise rudimentary structures which may lead to defects, aplasias, etc.; (3) obstructions—atresias—of parts which should have remained open. Through various combinations of these types there arise a large number of malformations. We will merely mention the various groups:

Simple Reduplication

The following types may be differentiated:

Incomplete Joining of Muller's Ducts (**fig.** 759).—(*a*) The otherwise well developed Muller's ducts do not join but develop in equal degree as isolated structures. This is the extreme of symmetrical reduplication of the uterus and the vagina (uterus didelphys s. duplex separatus). It is usually accompanied by other malformations such as the formation of a cloaca, or an abdominal wall-bladder fissure. From this extreme, there are milder malformations in which the well developed Muller's ducts are more or less incompletely joined, probably because of an anomaly in the round ligaments such as abnormal thickness or shortness (see lit. by Schottlander). These conditions may be further subdivided: From uterus didelphys or uterus duplex separatus there may occur: (*b*) uterus bicornis duplex; the uterus is completely doubled, both fundi diverge like clubs, below are the cervices, and, even if reduplicated, are still close together. The vagina may be double, but one horn may be atrophic (fig. 761).

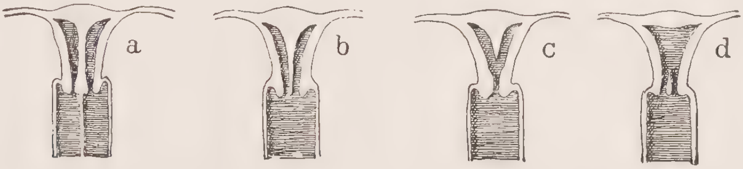


FIG. 759.—Diagram of double uterus caused by faulty adaptation of Muller's ducts; a, uterus didelphys or separate double uterus with double vagina; b, uterus bicornis duplex. There may also be a double vagina; c, uterus bicornis unicollis; d, uterus arcuatus, mere indication of bicornus.

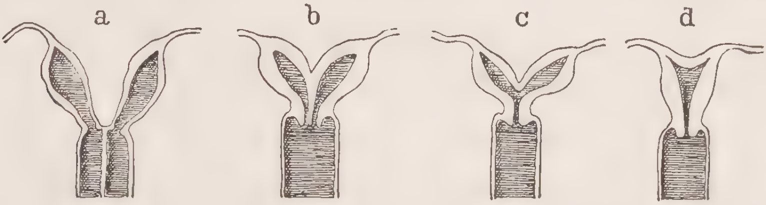


FIG. 760.—Double formations of uterus caused by defective fusion of Mullerian ducts; a, uterus septus duplex with septum of vagina; b, uterus septus duplex; c, uterus subseptus; d, uterus biforis.

(*c*) Uterus bicornis unicollis; the uterus is bicornuate, the cervix and vagina are single.

(*d*) Uterus arcuatus; there is a concavity at the fundus instead of the normal convexity, and this is the only indication of a bicornuate uterus.

Between (*c*) and (*d*) there are various degrees.

Incomplete Joining of Muller's Ducts (fig. 760). Muller's ducts join externally, but there is incomplete disappearance of the partition with formation of one canal. The uterus is normal to external appearances, but through the persistence of the partition, is divided into two cavities; the vagina likewise is reduplicated through a septum (*a*). This is the extreme degree of incomplete separation of the partition, the uterus septus duplex or uterus bilocularis cum vagina septa or duplici. From this extreme there are degrees of milder importance. Thus the uterus may be divided while the vagina is single, or, (*b*) the uterus is divided but asymmetrically and hemi-atretic, or is divided partly by the septum, and the vaginal wall reaches to the internal orifice (uterus septus unicollis), or (*c*) there remains only a trace of the partition in the fundus (uterus subseptus), or merely a scar or a fold which lies in the lower part of the uterus. Such ledges also occur in the vagina. Occasionally, only the cervix is divided by a septum, while the uterine cavity is single (uterus biforis). (*d*) A duplex vagina with a single uterus is very rare, (Marchand, Illner).

Aplasia (Complete Lack) and Hypoplasia (Rudimentary Formation) of Parts.—These malformations are found most frequently in the tubes, uterus and vagina; they do, however, also occur as aplasias and rudimentary developments in the ovaries.

Aplasia of Parts.—These follow arrest of development of Muller's ducts so that: (*a*) parts are incompletely developed on the right or left sides or both sides symmetrically, while above and below everything is normal. (*b*) In other cases, the agenesia involves only one Muller's duct. In the first case there occur symmetrical, in the last case asymmetrical aplasias.

(*a*) The highest degree of aplasia is represented by complete absence of the tubes, the uterus and the vagina. The next highest degree is total absence of the uterus; the vagina and external genitalia, as well as the remaining parts of the body may be completely normal. The tubes and ovaries may be present. In other cases, a part of the uterus is lacking; thus, *e.g.*, two horns may be equally developed, while the middle part and the cervix are not present; or the cervix is lacking, or parts of the vagina.

(*b*) As an extreme of asymmetrical aplasia there occur cases in which one Muller's duct is developed entirely normally, while the other does not develop at all (uterus unicornis). The developed horn is cylindrical, elongated and small, and leans towards the side from which the tube arises. There may also be, although not necessarily, an anomaly of the kidneys (fig. 669), usually unilateral lack of kidney, congenital cystic kidney or other such malformations (see Schilling, lit., and p. 1293).

Hypoplasias occur because Muller's duct does not completely develop, either bilaterally or unilaterally and asymmetrically on each side; there then occur symmetrical or asymmetrical structures of rudimentary kind. Thus the middle part of the uterus may be a solid muscle band; or it may be bicornuate, symmetrical or asymmetrical. The cervix, the tubes, or the vagina may be partly rudimentary. In a 19 year old suicide, the author saw defects of the right tube and the right ovary; the left ovary was small-cystic; the uterus, as large as a chestnut, symmetrical. If one horn of the uterus is rudimentary, there appears an asymmetrical uterus bicornis (fig. 761), and there may be differentiated a uterus bicornis with an entirely atretic (solid) cornua. If the cornua is entirely lacking, the uterus is unicornis. The rudimentary cornua may lie close to the uterus or be pulled away from this structure. It is composed of a solid strand which is elongated and may have swellings of muscle fibers, or is a small hollow body which may communicate with a cylindrical, well developed cornua on the other side. For orientation, the round ligament is useful, since it inserts into the rudimentary structure and lies below it. The tube on the side of the defect may be entirely normal or may be merely a solid strand. The ovary may be present or not. Occasionally, even if the ovary is present, it contains no follicles. The rudimentary cornua may be lined by mucous membrane as in a normal uterus and may take part in all physiological functions. If the mucosa menstruates, the blood collects

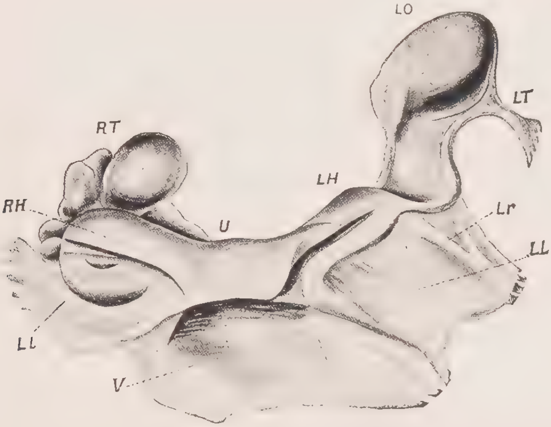


FIG. 761.—Uterus bicornis duplex, unsymmetrical with atresia of right cornua (RH); (U), middle part of uterus; V, vagina; LH, l. open cornua; the obstructed cornua has much thicker walls; LT, left tube with fimbriae; LO, l. ovary, much enlarged by a dermoid cyst with smeary fatty contents; RT, r. tube markedly distended by bloody fluid, much contorted; Lr, round lig.; Ll, broad lig.; drawn fr. fresh specimen; ⅓ nat. size.

and there arises a retention cyst, a hematometra in a rudimentary cornua (lit. by v. Klein). The tube may take up an impregnated ovum coming from the ovary belonging to it, or coming from external wandering of spermatozoa through the abdominal cavity, or possibly (very seldom) coming from the ovary on the open side, after external wanderings; here it may develop further (pregnancy in a rudimentary cornua). Through overstretching, but particularly because of growth of the placental chorionic villi into the wall, the horn may tear, so that hemorrhage and death occur, (see under extrauterine pregnancy). See Vischer, lit. for complete full-term pregnancy in the closed half of a uterus bilocularis.

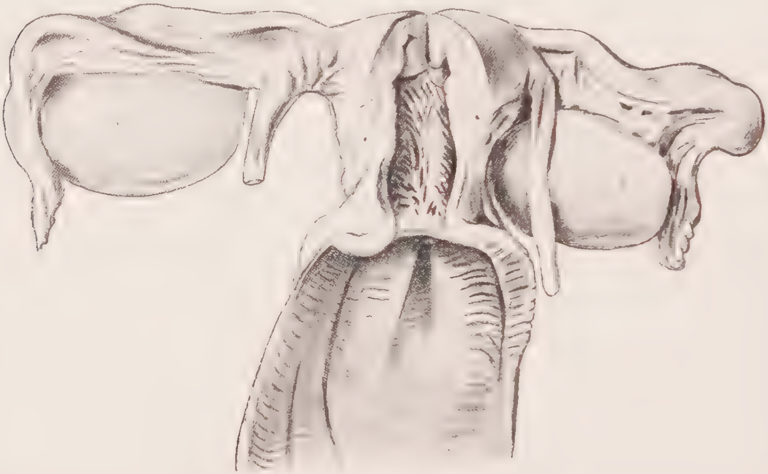


FIG. 762.—Hypoplasia of uterus; 18 year old girl with tuberculosis of lungs and intestines; circumference of aorta above valves 5 cm.; pulmon. art. 6.8 cm.; numerous fatty spots in the intima of aorta. Ovaries showed some small cysts. Body weight 28.52 kgs., body length 155 cm.; 7/8 nat. size.

A uterus which remains at the fetal stage is called a uterus foetalis; a uterus infantilis (fig. 762) is one which has not kept pace with the development of the individual. Normally, the uterus of the newborn has a thick, long neck and a very small corpus. Internally, the plicae palmatae, as the folds of mucosa are called, often reach to the fundus. From the sixth year onward, the uterus enlarges under normal conditions even though gradually and in small degree. At the time of puberty the enlargement is hastened, the body is larger than the cervix, becomes more massive, and takes on its normal anteflexed position in relation to the cervix by becoming sharply kinked anteriorly. In uterus foetalis this development is entirely lacking; in the infantile uterus it does not occur sufficiently, in fact, no development at all occurs at puberty. Often the remaining sex organs, particularly the ovaries, (lack of ovulation), and the breasts are poorly developed, or there is a poor development of the vascular system, or perhaps of the entire organism (as for example in cretins), and a retention of the child's habitus or figure.

Atresias.—In an otherwise normal uterus, atresias are rare. They occur most frequently at the external orifice and more rarely, involve the entire cervix. The vagina may be atretic in the neighborhood of the hymen, (atresia hymenalis). It is not always possible to say if the atretic place was always closed (solid), or whether it was at one time open and was closed by inflammatory processes during fetal life. These atresias are important at the onset of puberty since they lead to retention of the menstrual blood. Occlusion during pregnancy, particularly at the external orifice, and more rarely in the vagina or the hymen, is always acquired, (lit. by Ruge). Literature concerning stenosis of the vagina, both congenital and acquired, by Peters.

Among the rarities is the so-called connatal hydrocolpos, a tensely filled sac in the newborn, which may reach the size of a fist and which, connected with the cervical portion and a hydrometra as big as a hen's egg, may jut forward like a child's head. The sac occupies the entire breadth of the abdominal cavity and may reach to the diaphragm. The rectum is pressed flat; the urinary bladder and the urethra lie in front of the sac. The author has reported such a case, (so-called fetal rachitis, 1892, 9th. case). In a second case, the posterior surface of the urethra showed a slit-like horizontal opening, 0.8 centimeter above its orifice in the vestibule; a small sound could be passed through this opening into the hydrocolpos, but it was closed like a valve. This case, to be published in detail (Boehm and Hahn), may be classed as a hypospadius with deeply situated retrohymenal atresia, hydrocolpos and hydrometra (see von Rottkay, lit. and Kermauner).

Malformations of the Male Genital Apparatus

Testes and Epididymis.—Both testes may be lacking (anorchism). The entire habitus remains child-like, particularly the larynx. If one testis is lacking (monorchism), the other testis usually hypertrophies by way of compensation. The vas deferens and the seminal vesicles are usually present. Diminutive testes (microrchism) may be unilateral or bilateral. Hypoplasia is present when the testes are congenitally small and do not produce semen in their further development; this occurs in cretins (Langhans) and through the influence of congenital syphilis. Reduplication of a testis is rare; the double testis lies usually connected with a strand-like epididymis in one tunica vaginalis (Lossen, Merkel, Widhalm, Dransfeld). Dystopia testis transversa is the name given to the condition when both testes lie in one side of the scrotum (v. Winiwarter).

Disturbances of the descent of the testes (see Bramann): if one or both testes do not descend into the scrotum, the condition is known as cryptorchism or retentio testis. Unilateral cryptorchism is also called monorchism. The causes of these changes of position (dystopia) are varied: the testis may be retained in the abdominal cavity (lumbar or iliac) because of abnormal fixation through adhesions with the surrounding structures, or because its passage through the inguinal canal is obstructed by another organ, *e.g.*, the kidney (compare p. 1295). Very often, however, the testis is freely movable in a fold of peritoneum. The inguinal canal is almost always open (inguinal hernia). If the testis remains in the inguinal canal because the latter is too narrow, the condition is called retentio inguinalis (Uffreduzzi). The abnormal situation of the testis can be determined by sight and palpation. If the testis remains in the inguinal canal, its function, contrary to the views of Kuster, is not always preserved; in fact, it usually undergoes early atrophy (detail concerning the production of new interstitial cells by Finotti and Kyrle); the albuginea thickens, the interstitial tissue increases; it is prone to torsion (see below), to inflammations, and not rarely to tumor formation, (Finotti calls attention to the interstitial cells; see Wolf); at times, the latter occurs in an abdominal testis, and there have been cases reported in which the tumor weighed 9 pounds (lit. Blank, W. Fischer, v. Foth, lit.). The author described a large-cell left abdominal testicular tumor, the size of a child's head, in a 26 year old man. Malignant tumors of retained testes occur, even in children, (see the observation of the author, p. 1497). Retention of the testes is very frequent in children, but descensus usually occurs as the child grows older (Budinger). Separation of the testis and the epididymis, in which the former reaches the scrotum first, is rare. The author saw testis and epididymis with spermatic cord separated in an inguinal hernia; the testis as large as a plum lay above, the epididymis below in a small hernial sac.

If the testis, instead of descending to the scrotum, wanders into an entirely unnatural position, the condition is spoken of as aberration or dystopia or ectopia of the testis. It may be found in an entirely false place which is not in the path of normal descent, thus in the region of the perineum (Weinberger, Dangschat, lit.) or in the crural arch or in the folds between the scrotum and thigh. The ectopic testis usually undergoes atrophy; malignant change has also been observed.

Torsion of the pedicle of the testis, *i.e.*, the spermatic cord, with compression of the veins occurs occasionally, chiefly in youthful individuals; mild torsions are straightened out, but those lasting about two days lead to purple hemorrhagic infarction and necrosis of the entire tissue with subsequent cicatricial shrinking (Michael). The etiology may be: incomplete descent, too long a mesorchium, *i.e.*, fixation of the testis, or anomalies of insertion of the spermatic cord, too broad a tunica vaginalis and others, (see *e.g.*, the cases of Law, Righby and Howard, Lang, lit.); traumas, particularly overexertion, probably play an important role; in such cases perhaps there is a certain amount of torsion as a congenital condition (Murray). Torsion of the pedicle may also occur in an inguinal testis (Jastram, lit.); it may also occur with incarceration of a hernia. For thrombosis of the veins and hemorrhagic infarction not brought about through torsion of the pedicle, see Maschke.

If the testis is forcibly pushed into the inguinal canal or into the abdominal cavity, *e.g.*, by gymnastics, the condition is called luxation of the testis.

Prostate.—In unilateral or bilateral hypoplasia of the testis the prostate may be poorly developed. It may also be involved in epispadius with fissure of the bladder. See p. 1421 for so-called aberrant prostatic glands.

External Genitalia.—Anomalies of the prepuce consist chiefly of narrowing, (congenital phimosis), or the more uncommon total obstruction (atresia). Phimosis may be accompanied by an hypertrophy (hypertrophic phimosis); the foreskin appears as a long snout. The narrowness is caused chiefly by shortening of the inner layer. The prepuce and the glans are covered with epithelium almost until birth; in the epithelial masses are found many so-called epithelial pearls. These adhesions can usually be easily separated; if they persist the condition is known as congenital phimosis. Phimosis occasionally leads to the formation of preputial stones. Occasionally there occurs shortening (hypoplasia), or hyperplasia, seldom complete absence (aplasia) in an otherwise normal penis (Roth). Danziger has described two empty, blindly-ending prepuces

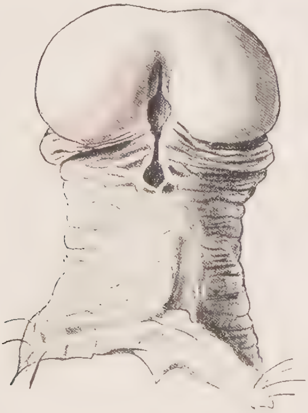


FIG. 763.—Hypospadius, older man; 7/8 nat. size.

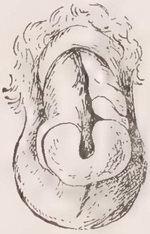


FIG. 764.—Epispadius of penis; urethral gutter in glans and penis; urethral meatus on symphysis. (After Ahlfeld.)

on the lower surface of the normal foreskinless penis. (Phimosis and hydronephrosis on p. 1407.)

The most important hindrances of development of the penis are hypospadius and epispadius. Hypospadius, lower or posterior fissure of the penis, was described on p. 1469. The milder degrees are relatively frequent, (according to Kaufmann, one in every 300 males); the more rare, higher degrees belong to pseudohermaphroditism. See Rumpel concerning hypospadius in one-ovum twins. See R. Meyer concerning hypospadius of the glans penis and its embryological importance. Epispadius is rarer than hypospadius. The urethra opens on the upper side of the penis. The mildest degree of this formation is the so-called ductus dorsales, which, coming from the urethra empties on the back of the penis (Stieda). There are differentiated: epispadius glandis, epispadius penis (fig. 764) and the highest degree, epispadius totalis, in which the hollow furrow runs along the back of the penis into the bladder; see p. 1424 concerning this latter condition, its frequent coincidence with extrophy of the bladder, and its genetic relationship. See p. 1424 for explanation of the origin of epispadius. [For epispadias in women (rare) and report of case, see Lower, W. E., Trans. Am. Assoc. G. U. Surg., Vol. 15, 1922.—*Translator*.] Entire absence, (aplasia), and failure of development, (hypoplasia), of the penis, when it resembles a clitoris, are rare; the former is usually an accompaniment of other severe defects of the external genitalia, while the latter is accompanied by hypospadius (Fischer and Steckmetz). Reduplication of the penis (diphallus) is exceptionally rare (Kuttner, Lange, Trenkler); there also occur diphallus partialis (1 shaft, 2 glans), see Heller. See R. Meyer, H. Albrecht (lit.), concerning the rare changes of position of the penis (under the coccyx, or in the perineum; clitoris under the posterior commissure).

See lit. by E. Konig concerning cysts on the under surface of the penis, some dermoid or epidermoid, some cylindrical epithelial cysts, originating from inclusions during the formation of the urethra, also concerning accessory passage-ways.

DISEASES OF THE MALE GENITAL ORGANS

Testes, Epididymis, Spermatic Cord and Its Coverings

(Embryology on page 1459 and forward.)

Anatomy. Physiology.—The testis is a gland composed of branching tubular canals. It is covered by the tunica albuginea or fibrosa, a tough layer which is a serosa covered externally by endothelium. On the posterior part of the organ the albuginea develops a connective tissue body which pushes into the parenchyma (corpus Highmori); from this, septa radiate like partitions into the parenchyma, dividing it into wedge-shaped lobules; it then inserts into the tunica albuginea. The convoluted tubules, with relatively strong laminated walls, compose the chief mass of each lobule; after a short course they pass as narrow tubules into the body of Highmore and communicate with a narrow network of epithelial tubules without walls, the rete testis (rete Halleri). Then they leave the body of Highmore in the form of about 15 vasa efferentia with tough walls; these, strongly convoluted, are called the coni vasculosi, which form canals grouped in lobules; the entire structure composes the head of the epididymis. These canals join to form the vas epididymis, which is much convoluted and comprises the body and the tail of the epididymis; in its further course, it is called the vas deferens. The epididymis lies on the posterior edge of the testis; the head is above, the tail below, the middle part is the body. The vas deferens leaves the tail, turns, winds in back of the testis to the inner side of the epididymis, passes upward and then follows the spermatic cord into the abdominal cavity (see fig. on p. 733). The thick walls of the wide contorted tubules are composed of a number of layers of flat connective tissue cells, and a fine membrana propria covered by layers of epithelium. The latter are differentiated into two kinds of cells, Sertoli's cells (in contrast to the germinative cells they are also called vegetative) which have nothing to do with the formation of the semen, but which, according to Hanes, supply fat necessary in the development of the seminal cells, and the spermatogonia, from which the spermatocytes of the first and second order arise; these afterward become the spermatids, and these in their turn become spermatozoa. The narrow straight tubules consist of a membrana propria and a simple layer of low cylindrical epithelium. The canals of the rete are lined by a simple layer of small cuboid or flat cells. The tubules of the epididymis (the vasa epididymis) have a single layer of high ciliated epithelium with supporting cells between, a striped basal membrane and several layers of muscle.

The head and anterior part of the body of the epididymis are covered by the same serosa which covers the testes, *i.e.*, by the visceral layer of the tunica vaginale propria. With the parietal leaf it forms a closed serous sac (cavum scroti), known as the external part of the processus vaginalis peritonei, with which we became acquainted during the descent of the testes (p. 731). External to this is the tunica vaginalis communis, a fibrous covering surrounding the tunica vaginalis propria and the epididymis (fig. B, p. 733).

The testis and the epididymis together are called the "testicle" (Waldeyer and Joessel).

The interstitial cells (Leydig) are connective tissue cells of epithelial contour, which lie between the seminal tubules, and vary considerably in number in individual cases. They are said to be analogous to the lutein cells of the ovary. They are very numerous in the fetus; in the newborn, they contain much fat; after the age of puberty, on the contrary, the cells of the seminiferous tubules contain this substance (Hansemann, lit. by Herxheimer), and especially, according to Hanes and Rosenbloom, Sertoli's cells; they disappear in boyhood, to increase again at the time of puberty; they then decrease, to increase again in older age (see also Kasai). Their function is still hypothetic: – trophic, assisting organs (Plato), which see that the cells of the seminiferous tubules reach their functional height (Kyrle, Tiedje, Leupold and others); cells which may act vicariously for the spermatozoa (Simmonds); space-filling supporting tissue (K. Koch); storage places and depots for the hormone formed in the spermatogonia (Berblinger); organs of internal secretion of the testes and therefore determining the secondary sex characteristics (type of breast, voice, larynx, pelvis, etc.), as concluded by Tandler and Grosz from animal experiments. With Steinach, Lipschutz calls them the male "puberty glands," which determine the secondary sex characteristics in direct ratio to their development. (The female "puberty glands" are said to be the interstitial ovarian glands.) But Kyrle has questioned the importance of animal experiments thus far done, and the investigations of Stieve especially, have cut the ground from under them; according to the latter, the interstitial cells have only a trophic function; the secretion of a hormone from the interstitial cells has not been demonstrated, and the development of the secondary sex characteristics is dependent on the genital part of the testes (see also v. Keussler); through its sex cells the testis determines the essential sex characters (see Pick). See also literature in appendix.

The interstitial cells may contain Reinke's crystalloids which are thick, straight, or slightly bent rods, considerably larger than the nucleus. Charcot's crystals can also be found in the different epithelial cells of adult testes. Small slender, needle-like crystals (according to Cohn, crystalloids) were found by Lubarsch in the spermatogonia of adults; but Spangaro, confirmed by Thaler, found these testicular crystals at every age, even in children. Finally there have been found bacillus-like crystals only in Sertoli's cells, from the time of puberty onward (Spangaro, lit.). The meaning of these structures is unknown (for illustrations, see Cohn). There also occur general diseases in which spermatogenesis is decreased and in which the interstitial cells increase in number, thus, markedly in the atrophic testes of cachectic individuals, as in chronic tuberculosis, senility, carcinoma, nervous diseases, alcoholism (Bertholet, Langhans, Hansemann, Lubarsch, Durck, K. Koch), and also in experimental atrophy of the testes following x-ray, exposure (Herxheimer-Hoffmann, Simmonds, Kyrle), in which, according to Simmonds, the increased interstitial cells undergo atrophy when the destroyed seminiferous tubules are regenerated. They are often found, although not always, (see Schoppler, Berblinger, Sternberg and others), in cryptorchid testes (Finotti, Felizet and Branca, Pick, Chevassu, the author), as well as in internal masculine pseudohermaphroditism (Stroebe, Pick, the author), in which the collections may form macroscopic nodules. The author has observed an actual tumor-like enlargement of the testes in brothers, *i.e.*, a tumor from overgrowth of interstitial cells; the case has been briefly described by Hansemann and Durck who also saw overgrowth, but limited to the interstitial cells in diminutive testes. Poll describes similar tumors in avian hermaphrodites (see also Stoppato, whose case A. Frank, however, believes shows large cell epithelium). Marked pigmentation of the interstitial cells occurs in pernicious anemia, and in general hemochromatosis (p. 928), as well as in other conditions, and the testes appear brown on section.

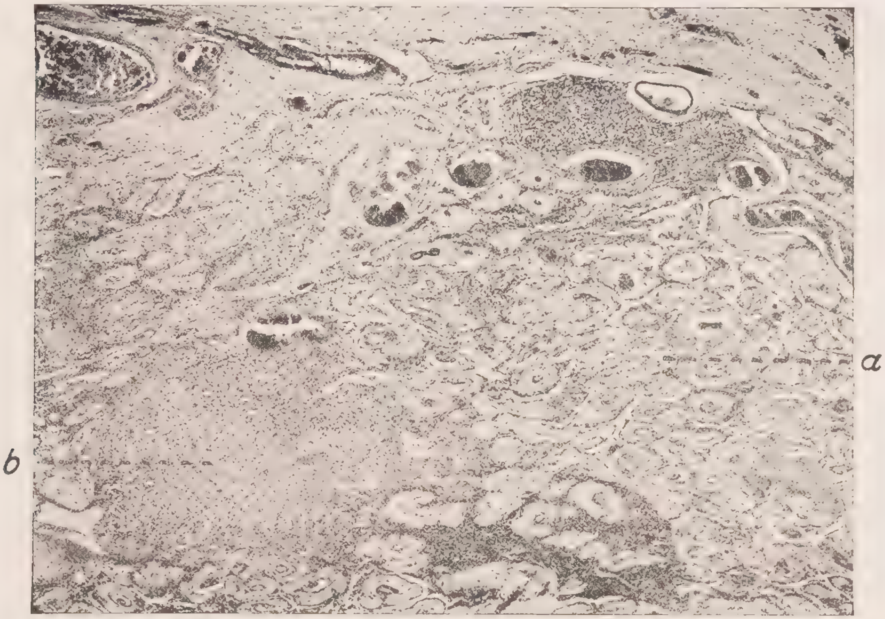


FIG. 765.—From the testis of a case of complete masculine pseudohermaphroditism from servant girl 46 years old. Hyalin seminal tubules (a), larger groups of interstitial cells (b). (× 35.) (After Moller, V. A. 223, 1917.)

Concerning relationships between the adrenals and the testes, such as a constant size and weight relation of both organs (testes to adrenals as 2½ is to 1), parallelism between the fat content in the adrenals and the interstitial cells, degeneration of the seminiferous epithelium, a change which occurs in all serious diseases of the organism, after experimental removal of the adrenals and others, consult Leupold, who calls attention to the importance of the secreted cholesterin ester of the cortical parts of the adrenal for the regular occurrence of spermatogenesis, and furthermore, to the influence of the work of the thymus and the adrenals on the normal development of the testes. See also p. 1279. Berblinger calls attention to correlation between the interstitial cells and the hypophysis; a hypofunction of the latter organ is said to retard the activity of the interstitial cells.

The much discussed experiments of Steinach consisted of rejuvenation of the senile puberty glands after ligation of the efferent duct of the testes; after regression of the seminiferous epithelium with retention, there was overgrowth of the interstitial cells. This, occurring in rats, is said to have yielded isolated similar results in humans (v. Lichtenstern, Schmidt, Littauer). Many, of course, believe the human effect was due to subjective phenomena and autosuggestion (see Freudenberg, Lick), and have denied there was any actual rejuvenating influence even after the implantation of interstitial testicular tissue; but they do admit the possibility of a transitory, erotic effect. Kyrle denies the value of the animal experiments on which Steinach's hypothesis rests; in Fahr's experiments with dogs, there occurred no increase of interstitial cells. According to Tiedje, the interstitial cells undergo hypertrophy because of increased absorption of albuminous substances from the degenerated genital cells. Simmonds saw retention of spermatogenesis after atresia of the vas deferens, and in 40 human cases, saw increase of the interstitial cells but twice. Verocay (lit.) saw a congenital defect of the ductus deferens, with spermatogenesis even up to the 73rd year of life. All these things cannot be correlated with the teaching that an increased libido (so-called rejuvenation) is a result of hyperfunction of increased interstitial cells.

In homosexuals, Steinach described cells in the connective tissue between the seminiferous tubules which could be distinguished from the remaining neighboring interstitial cells by their size; he called them "female puberty gland cells, (F-Zellen)," and since there was a diminished development of interstitial cells of the male type, these of the female type determined the libido of the homosexual for the same sex. But these lutein-cell-like structures, as found by Steinach, are believed by Kyrle to be but variations of the interstitial cells which can be found in other individuals. When Steinach builds up the further hypothesis, that this female influence may extend even to producing somatic female characteristics, such as breasts, hips, female form of pubic hair, etc., his theories are confounded by other findings; see, *e.g.*, those of Schmincke and Romeis in a male hermaphrodite, in which they could demonstrate no increase of "F cells" which were expected according to Steinach's hypotheses; in fact, they were not more numerous than in normal testes. They showed, furthermore, that these interstitial cells were merely older Leydig's cells containing typical brown pigment. Finally, Schmincke and Romeis disagree with the conception of "puberty glands" as promulgated by Stieve, and do not believe that pseudohermaphroditism is due to an interstitial hermaphroditic sex gland, but agree with Kermauner that the cause of pseudohermaphroditism is a local malformation. The possibility of bringing about bisexual and homosexual characteristics by the transplantation of testes has been denied by Stabel; on the other hand, such implantations in those who have been castrated late in life were followed by renewed libido and potency (see also Kreuter). Cryptorchid human testes have been used for such implantations, especially inguinal testes.

For malformations of the testes, see pages 1475 and 1476 and literature by Herxheimer.

According to Kyrle, developmental disturbances of the male sex organs in youth are very frequent; in 110 individuals up to their eighteenth year, he found normal testes in merely 10; in all of the others the testes were poorly developed. Increase of the interstitial tissue occurring after puberty is, according to Kyrle, a permanent stigma, and a certain amount of diminution in function is said to have resulted. (Concerning the question of diminished development, see also W. H. Schultze and Mita, Voss, Kyrle.)

In the injured epididymis of animals, Kyrle and Schopper saw marked proliferation and regeneration in the region of the wound, whereby new tubules arose; Kyrle also obtained extensive new formation of tubules coming from the rete testis.

Testicular Hemorrhages.—Those occurring from torsion of the spermatic cord with hemorrhagic infarction have been mentioned on p. 1476. Small petechiae in the parenchyma of the testes are not uncommon in the hemorrhagic diatheses, both essential and septic, particularly in streptococcic infections. Traumata may lead to destruction of tissue and hemorrhage.

Simmonds has described the frequent birth injuries consisting of hemorrhages in both testes and epididymi which occur when the head is born and the body is tightly constricted by the introitus vaginae; he believes they are of medico-legal importance as signs of asphyxia. There is often a coincident edema of the scrotum.

Acute and Chronic Inflammations of the Testes and Epididymis.—Inflammations of the testis (orchitis) and the epididymis (epididymitis) occur most frequently through spread of an inflammation from the neighborhood, *i.e.*, from the tunica vaginalis, the spermatic cord through the vas deferens, from the urethra, the bladder, particularly after catheterization, in bladder paralysis, hypertrophy of the prostate, etc. Those inflammations ascending through the spermatic cord involve first or only the epididymis, which becomes a thick nodular mass shaped like a helmet. The chief cause is gonorrhea, but occasionally other severe inflammations of a suppurative or gangrenous form may follow operations, such as removal of stone from the bladder, stricture, etc.

In other cases, subcutaneous or cutaneous traumata are the causes of inflammation, particularly in the epididymis. Mild traumata such as squeezes, tears, pulls, fast walking, riding, etc., even a poorly fitting suspensory, favor the spread of gonorrhea to the epididymis. Hematogenous inflammation of metastatic type may involve one or both testes, occasionally the epididymis also, *e.g.*, in pyemia, (staphylococcus and other pyogenic organisms), in mumps (p. 594), scarlet fever, typhoid fever (in which there are round cell masses, Mallory, and toxinogenous masses of necrotic cells in the interstitial tissue, Fox), cerebrospinal meningitis, pneumonia and syphilis. Fulci described an acute interstitial orchitis in rheumatism (compare orchitis fibrosa, p. 1485). In variola, there are almost always focal infiltrates in the testes which lead to epithelial necrosis (Chiari); according to Simmonds, these necrotic masses later disappear and leave shrunken scars.

In acute gonorrheal epididymitis, there are round cells, desquamated epithelium, mucoid and fibrinous exudate in the tubules. The epithelial layer and the subepithelial connective tissue are infiltrated by leucocytes. The disease may heal with complete resolution. Severer changes consist of granulation masses containing, among others, many plasma cells; after destruction of the original epithelium, the new cells change their character and develop many layers which jut into the lumena of the tubules (for more details, see Wolf, lit.). Not rarely, the vas epididymis is likewise involved, perhaps destroyed by suppuration (Baermann). The interstitial tissue is infiltrated by round cells and saturated with exudate, the swelling depending on the amount of the latter; occasionally, according to Smith, relatively frequently, there appear small abscesses (Nobl). A hydrocele usually results. Abscesses leave nodular scars. The elastic fibers disappear in the pus. Pus cells in the interstitial tissues and tubules of the epididymis are the rule in pyogenic infections by staphylococci and streptococci and abscesses of varying size are the result. In chronic epididymitis connective tissue is added, leading to nodular thickenings, and deposition of calcium salts. Shrinking of the connective tissue obliterates the vas epididymis, or blocks secretion with subsequent cyst formation. When the spermatic cord is destroyed, or the epididymis is indurated, as in gonorrhea, secondary soft connective tissue flecks, and exceptionally, a diffuse connective tissue infiltration appear in the canal of the testes, but tough scars following interstitial inflammatory processes are rare (Simmonds). Consequences: obliteration of both vasa epididymi, and azoospermia, since the seminiferous tubules cannot be emptied. In spite of the continuation of spermatogenesis and the libido, the individual is sterile (impotentia generandi).

In acute orchitis, the testis swells and becomes very hard to palpation. Exudate appears in the tubules and interstitial tissue, but the latter is more involved than in an epididymitis. In suppurative inflammation, to which the testis is more subject than the epididymis, the tubules are filled with pus, and when the infiltrated interstitial tissue is liquefied, abscesses appear in numbers. Traumatic orchitis usually is suppurative and phlegmonous.

Course of the Abscesses.—Small abscesses, after absorption of the pus, heal by scar tissue; larger abscesses usually leave pulpous cholesterin-rich debris surrounded by connective tissue (atheroma of the testis); occasionally these residues are calcified. They may penetrate the tunica vaginalis and rupture through the outer skin, broadly or through a fistula; bluish red granulation tissue like fungi then grows out at the opening. When the process heals, scarred depressions are left.

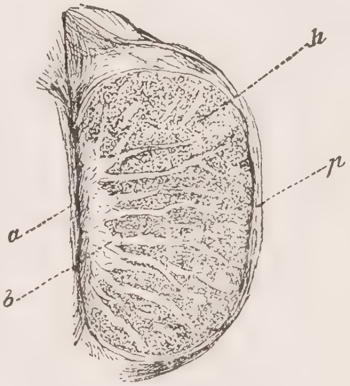


FIG. 766.—Fibrous orchitis from a syphilitic man with other symptoms of old syphilis. a, corpus of Highmore from which branching thickened septa (b), radiate into the parenchyma (h); p, thickened albuginea; scrotal cavity obliterated; nat. size.

Fibrous Orchitis.—Wherever a primary epithelial degeneration or an inflammatory exudate is healed by connective tissue overgrowth or by scar tissue, there is a fibrosis; this is manifested in the testis by white flecks and stripes. The connective tissue is tough and sclerotic, or soft, tender, reticular or mucoid.

Remnants of atrophic tubules and atypical epithelial overgrowths may resemble carcinoma.

Simmonds recommends the name "fibrosis of the testis" for all forms of fibrous change of the parenchyma, whether it be as a residuum of an inflammatory or a purely degenerative process, a true scar, or only a focal relative increase of the interstitial tissue (soft fibrosis) after destruction of a few tubules.

When an orchitis, beginning as an acute inflammation, lasts for some time, it takes on an indurative character (fibrous chronic orchitis), and the growing interstitial tissue destroys the parenchyma. But in syphilis, acquired as well as congenital, fibrous induration may arise independently.

This has been called simple syphilitic orchitis in contrast to the gummatous variety, even though all combinations and direct transitions between both types occur. The small septa are often changed into heavy branched partitions which radiate like fingers from the corpus Highmori or from the albuginea. In other cases, there are larger scar-like, rounded or striped flecks, or the entire section surface retains merely a few brown remnants of parenchyma in a scarred moist white tissue. There is often an adhesive or an exudative periorchitis coincidently present. Microscopically, the connective tissue overgrowth is found infiltrated with small cells; some of the tubules are entirely destroyed, but others show varying degrees of contortion, kinks, hyalin thickenings (fig. 771), narrowing and total obliteration; the epithelial cells undergo fatty degeneration. The elastic fibers of the tubules may be preserved for a time, even though present in clumps and irregular bundles, except when such a scar has resulted from an abscess which has destroyed the elastic fibers. True gummata heal to rough scars, in which new elastic fibers may be deposited (Federmann.) The end result of this interstitial or fibroplastic orchitis is a non-characteristic tough cicatricial connective tissue (fibrosa).

According to Eug. Fraenkel, so-called "orchitis fibrosa interstitialis" may also be initiated by primary degeneration of the epithelium, followed by thickening of the walls and obliteration of the tubules, *i.e.*, by scar formation following a spermatoangitis fibrosa obliterans. But this occurs not only in syphilis, but also in various infectious diseases such as gonorrhea, tuberculosis, rheumatism, and intoxications such as alcoholism and others. There is nothing pathognomonic of syphilis in these cicatricial changes, even though they occur more frequently from this than from any other condition. (See Eug. Fraenkel and Much concerning the Wassermann reaction in orchitis fibrosa; in 13 cases it was positive twice; and contrariwise, Lohlein and Schlimpert, Simmonds (lit.), the latter of whom obtained 12 positive reactions in 20 cases.) If the Wassermann reaction is positive, it merely says that the individual probably has syphilis, and does not necessarily mean that the observed testicular scars are of syphilitic genesis.

"Fungus benignus testis," is granulation tissue growing like a sponge at the surface of a fistula of the skin of the scrotum and the testis; it arises in various ways: (*a*) when the tunica vaginalis is opened by a penetrating wound, the intact testis partly prolapses, and the surface of the testis (albuginea) yields granulation tissue which forms the fungus (fungus superficialis); (*b*) when albuginea is also severed, seminiferous tubules prolapse from the opened testis and are destroyed; from the depths of the testis there grow granulations; (*c*) through processes as described on p. 1485, abscesses, ruptures, growth of granulations from the abscess walls; (*b*) and (*c*) are called fungus profundus. Other forms of fungus testis are specific, such as tuberculous, (p. 1490), or, less often, syphilitic (p. 1493); others are malignant, *i.e.*, perforating sarcomas or carcinomas.

Infectious Granulation Tumors of the Testis and Epididymis. Tuberculosis of the epididymis and testis is frequent. It occurs in children; thus the author saw tuberculosis in a 1 year old child; Cholmeley saw tuberculosis of the testis in a 6 months old boy. On the other hand, the disease has been seen in extreme old age. Very rarely, it is the only tuberculous focus in the body (primary tuberculosis), when, as a rule, it begins in the epididymis. But, more often, other organs such as the lungs, and intestines are also involved; the testicular tuberculosis is then hematogenous in origin.

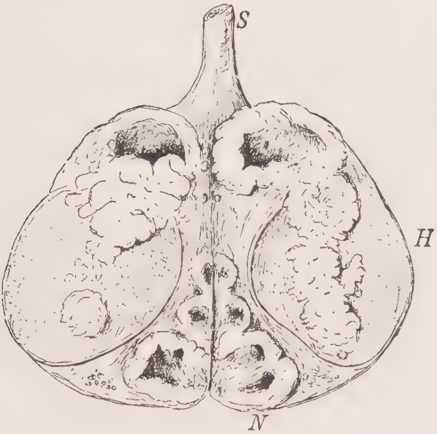


FIG. 767.

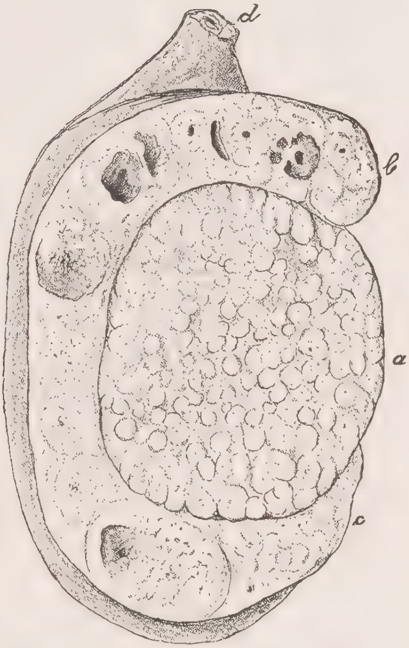


FIG. 768.

FIG. 767.—Caseous cavernous tuberculosis of r. epidydimis (N) extending to the testicle H; S, spermatic cord; man 55 years old with urogenital tuberculosis and tuberculosis of lungs (peribronchial, no tbb in sputum); intestinal ulcers; also a stenosing carcinoma of pylorus; ¾ nat. size; drawn from fresh specimen.

FIG. 768.—Rare form of tuberculosis of epididymis and testicle. The first contains numerous softened caseous nodules; many irregular lumena of the thickened caseous vas epididymis are still recognizable; b, head; c, tail of epididymis. In the testicle (a) also irregular lumena (tubules dilated by caseous disintegration), surrounded by caseous rings; d, vas deferens within spermatic cord. Removed from a man 55 years old whose other testicle was removed on account of tuberculosis some years before. There were several fistulae, not visible in this half of the specimen; nat. size.

Sussig has called attention to the importance of hematogenous, genito-primary tuberculosis of the epididynis and testes; tubercle bacilli were found inside of the tubules only when histological rupture was present of tuberculous masses from without. Benda does not believe that there ever occurs a primary hematogenous epididymis tuberculosis; he believes it always comes from the seminal vesicles or the prostate.

Occasionally, it appears during the course of a general tuberculosis of the body, in which, especially in children, disseminated tubercles may be found, particularly in the testes; through quick spread and rapid destruction of the interstitial tissue, they form thick caseous nodules; fistulae, however, are rare (Broca). For more details concerning hematogenous tuberculosis, see p. 1490.

Tuberculosis of the epididymis and testes is often concomitant to chronic urogenital tuberculosis; the vas deferens, seminal vesicles, prostate, bladder, ureters and kidneys may all be involved, or any one of these. The process is usually spread from the epididymis to these organs, and less frequently, vice versa.

In tuberculosis of the sex glands, the epididymis is involved first, as a rule; it may be enlarged as a nodule or a thick sausage-shaped mass, or may rest on the testis like a helmet, almost destroyed by caseation which still allows recognition of the lumena of the canals (fig. 768); this is often before there are more than a few small nodules in the corpus of Highmore and in the parenchyma of the testes themselves. If the epididymis is markedly diseased, however, the testis is almost certain to be involved (fig. 767); in mild cases, the latter may remain healthy.

The beginning of the process in the epididymis (usually in the tail), is, as a rule, in the epithelium and the walls of the tubules, and much more rarely in the interstitial tissue, while tuberculosis of the latter is considered ordinarily of hematogenous origin (p. 1490). The tuberculous growth, therefore, is established in the tubules, where there are soon visible sharply outlined, often reticulated tubercles containing giant cells. (These, according to the older views of Langhans, are of epithelial origin, but, according to Lotsch, are of non-epithelial origin.) Within them, the elastic fibers, which are the scaffolding of the tubules, disappear; the whole structure then undergoes caseation, neighboring tubercles become confluent, and the inner layers of the tubules are destroyed. The entire mass finally becomes mere caseous material which fills the lumena, while the walls, through the formation of new tubercles, become much thickened. Thus the peritubular tissue is involved, and isolated miliary nodules appear in the interstitial tissue. On section, the caseous vas epididymis appears as holes with caseous walls surrounded by a glassy gray red thick mantle or ring; the more the caseous process increases and brings about softening, the larger and more irregular are the lumena of the tubules. If the process becomes older, cicatricial masses are established in the neighborhood. Occasionally the caseation involves the entire epididymis, and cavities are formed through softening; they are filled with caseous debris and lined by an irregular villous wall (figs. 767 and 768).

The testis may remain unimpaired, but this must be determined by microscopic examination (v. Brunn, lit., Samuel); if the process does spread to this organ, further dissemination of tubercle bacilli takes place through the seminiferous tubules or through the lymph tracts. The former is probably more frequent, for on the inner surfaces of the tubules and in their walls, tuberculous tissue can be seen (tubular tuberculosis). The tubercles sometimes form chains around the tubules, their localization determined by the lymph channels. In addition to this localized intra- and pericanalicular arrangement, there are tubercles here and there in the interstitial tissue; the parenchyma, through enlargement and confluence of the tubercles, is destroyed or locally compromised, brought to fatty degeneration, and overgrowth. Usually the number of isolated conglomerate tubercles is limited; in the beginning they are somewhat rounded, soft and gray red, they caseate from their centers outward and then become firmer, but seldom any larger than the seed of a cherry. The firm masses may soon soften (Federmann), but it is quite difficult to determine, even microscopically, whether the soft areas were at first firm. The macroscopic impression is, of course, that of softening. But a spread by continuity of caseous masses from the epididymis to the testis is not rare (fig. 767). Occasionally there is total, homogeneous, stiff caseation without a trace of architecture on the section surface, and with great enlargement even to the size of a goose egg, and even, as a preparation in Basle shows, involving both testes.

It is only in very chronic cases that there occasionally occurs a uniform caseous tuberculous overgrowth into the walls of all the testicular tubules, as in fig. 768. The very small rounded cross sections of tubules may easily be mistaken for miliary tubercles, but there is a small irregular opening in their centers.

A very unusual form of fibrous change in a tubular tuberculosis was seen by the author in the left testis of a 42 year old man with extensive urogenital tuberculosis (kidneys, ureters, seminal vesicles, prostate, urinary bladder, urethra); the left testis was caseous, cavernous and fistulous. The cross- and longitudinal sections showed obliterated white tubules, changed by fibrous tissue with slight depressions in the centers, and infiltrated by a fine fibrous network; the tubules were 2–3 mm. thick, radiating from the corpus of Highmore in thick groups into the remaining soft parenchyma. Similar pictures were found by the author in other cases, and may be seen in testes which still show caseous masses. See p. 1487 concerning spermatoangitis fibrosa obliterans, which, according to Eug. Fraenkel, may be caused by the liberation of toxins from tubercle bacilli in other organs; see to the contrary, Simmonds.

Hematogenous tuberculosis of the testes occasionally occurs in the form of one or more larger caseous nodes. In generalized miliary tuberculosis, on the contrary, typical interstitial miliary tubercles are common; they finally reach the walls of the tubules and occasionally prefer the subalbugineal layer. The epididymis is usually intact (see also Benda). Isolated hematogenous miliary tubercles may probably heal by way of connective tissue. See p. 1488 concerning hematogenous tuberculosis in children.

In young chronic phthisics, the testes are often poorly developed.

See p. 1492 for the microscopic differential diagnosis between tuberculosis and syphilis of the testes. Sporotrichosis (see under skin) may also produce changes in the epididymis, clinically similar to tuberculosis (see Arndt).

When secondary nodules appear in the tunica vaginalis, there is exudative inflammation. When the parietal layer,—the tunica vaginalis communis,—and the subcutaneous scrotal tissue is also invaded, the progressive caseation and softening finally reach the surface (tuberculous fistula of the testis). Rupture, however, seldom takes place through the tunica vaginalis propria, but through parts not covered by serosa and from a soft caseous cavity in the epididymis, usually in the head, or in the corpus of Highmore. But the fistulae may also lead into a cavity in the testis. When tuberculous granulation tissue grows around the opening, it constitutes a tuberculous fungus of the testis, perhaps as large as a hen's egg.

The discovery of tubercle bacilii in the tubules of the testes and seminal vesicles of otherwise healthy testes in tuberculous individuals (Jani, Spano, Jakh, Nakarai) was not confirmed (Sussig, lit.); this discovery was the chief support of the so-called excretion tuberculosis theory, and was believed to be the explanation of testicular and epididymis tuberculosis found in phthisical individuals following trauma and acute inflammations, particularly gonorrhea. According to Sussig, however, excretion occurs only when there is rupture of interstitial tubercles into the lumena of the tubules. After crushing a testis in rabbits, Simmonds obtained epididymis tuberculosis after injecting infected sputum into their abdominal cavities. In dogs, Asch found sclerosis of the testis following injections of tuberculin into the spermatic artery. Kramer (v. Baumgarten) obtained tubular testicular tuberculosis following injections of pure cultures of tubercle bacilli into the vas deferens. Von Baumgarten stated that the tuberculous process always followed the direction of secretion, *i.e.*, from the testes toward the prostate, from the kidneys toward the bladder, and never vice versa; but after repeating his experiments, he convinced himself that the reverse route is also possible (see also Voelker). The author has come to this opinion on the basis of autopsy findings, and believes that stasis of secretion is an important predisposing cause; with Enderlen, he obtained experimental results in rabbits and goats, which prove this possibility. See also the literature cited on p. 1431 under tuberculosis of the bladder, and compare tuberculosis of the prostate. See also Sugimura, Pratorius.

Syphilis.—In contrast to tuberculosis, which, as we have seen, particularly involves the epididymis, syphilis chiefly involves the testis itself. Testicular syphilis occurs in the later stages, but also in the newborn in the forms of interstitial orchitis and gummatous infiltration. (Lit. by Herxheimer, E. XII. 1908, page 568 and following.) Two chief forms may be differentiated, but they are often combined: (*a*) **fibrous orchitis,**—fibrosis testis syphilitica,—result of a primary interstitial fibroplastic orchitis mentioned on p. 1487. The condition has nothing specific about it, and its syphilitic nature must be recognized from the microscopic examination, the history and the entire aspect of the case or the autopsy. The testis is usually not enlarged; on the contrary, is small and hard; the epididymis is usually intact. (*b*) **Specific, gummatous orchitis.**

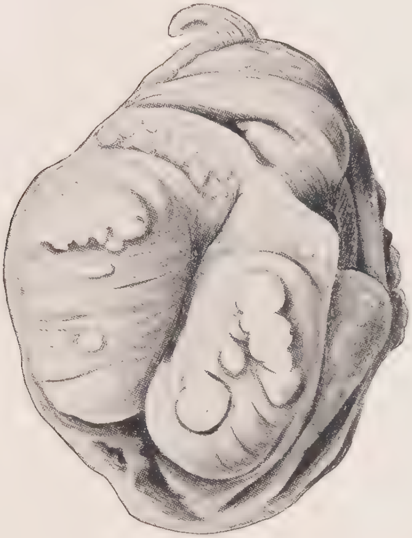


FIG. 769.—Gummatous orchitis; man 30 years old. The firm gummatous areas project above section surface. Operat. spec. taken to be a sarcoma; the other testicle similar; 7/9 nat. size.

The late stages are those most frequently encountered in the form of scarred gummatous orchitis; the enlarged, tough, approximately egg-shaped testis on section is a fleshy pale gray red or tendinous white or brown blood-pigmented structure, showing somewhat prominent rounded or rounded-angular or map-like, rather tough gummatous nodules as large as peas, beans or hazel nuts, seldom as large as walnuts. They are embedded in a dry, homogeneous, opaque, pale yellow (caseous) tissue, or one which shows yellow or brown stained rims around necrotic parts (the latter an early stage) and which show necrotic masses only in isolated internal places, and not, as a rule, softened. The peripheries may be adherent, or may be encapsulated by connective tissue. Younger gummas are white, glassy, dirty-gray-red or yellow-brown and found more frequently in early cases with very little other change in the testicular tissue. The entire testis may finally be cicatrized. The epididymis is usually not differentiable, and may likewise be scarred and gummatous. The tunica vaginalis is thickened; its cavity is obliterated, as a rule. Gummas tend to be tougher in the testes than in other organs.

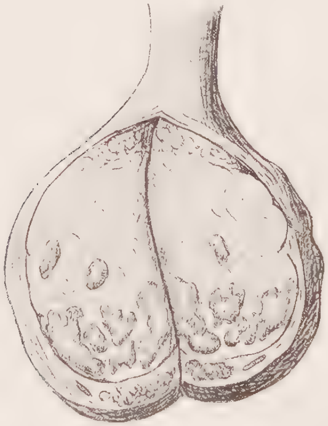


FIG. 770.—Fibro-gummatousorchitis with fibrous epididymitis, thickening of the tunica vaginalis and obliteration of its cavity. From the cicatricial tissue project numerous gummatous nodules, mostly close to the albuginea; nat. size.

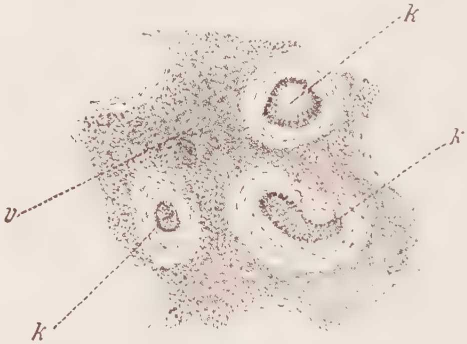


FIG. 771.—Gummatous orchitis, from the edge of a gummatous nodule. K, atrophic seminiferous tubules with hyalin walls; in between gummatous granulation tissue; caseation at v. (Medium magn.)

Microscopically, younger gummata, before caseation begins, show rounded spindles and epithelioid cells. The interstitial glandular tissue gradually undergoes atrophy (fig. 771), the elastic fibers are spared, and thus the rough contour of the convolutions of the tubules is retained. In older gummas, there is a preponderance of a fibrous spindle-cell tissue undergoing necrosis, and filled with fat droplets, cell detritus and cholesterin; the formation of giant cells is usually minimum. Changes in the vessels are always present; (compare the microscopic picture of a gumma, under muscles, fig. 993, and the differential diagnostic criteria from tuberculosis on that page, as well as the observations on p. 1489). In contrast to most tuberculous caseous masses, the elastic fibers are preserved in older dry gummata, so that there are still suggestions of the contours of the walls of the tubules (Orth, Federmann). This finding may be of importance in the differential diagnosis (p. 1486), although not in all cases, since the elastic fibers in some syphilomata also undergo degenerative changes. In the middle of a cellular tubercle, the elastic fibers always quickly undergo destruction, and it might be remarked, that it is at this stage when the cells are well preserved, and not during caseation of the tubercle, that the damage is done to the elastic fibers. If the canalicular form of tuberculosis is established, as it is in most of the cases, the elastic fibers of the tubules are destroyed and retained only in the interstitial tissue. When the intratubular tuberculosis has proceeded to caseation, these run between caseous tubules. If the much rarer interstitial (intertubular) testicular tuberculosis has developed, the elastic fibers are long, even though not permanently recognizable in their tubule-like arrangement. If a gumma finally undergoes softening, or if suppuration sets in, the elastic fibers disappear, although softening is usually only partial; the non-softened areas then give a clue to the diagnosis (Federmann). Naturally, staining for tubercle bacilli is a useful procedure. v. Baumgarten believes that an important point is complete absence of typical Langhans' giant cells, but we cannot agree with him; he also believes that the blood vessels with their contents are fairly long preserved in a syphilitic new growth, which the author can confirm.

Enlargement of the egg-shaped organ, occasionally the size of a fist, depends either upon the presence of particularly many, or very large, gummata, (exceptionally, as large as a goose egg), or on marked connective tissue overgrowth. (Danger of mistake for tumor! Gummata are usually painless.) Gummata of the testes, in contrast to tubercles, have very little tendency to softening; caseation occurs much later than in tubercles. If, however, softening does occur, similar cavities appear in the gummata and fistulous communications into the scrotal tissue and to the exterior; gummatous masses then grow from the fistulous opening as a fungus syphiliticus (very rare!). Gummata may disappear completely through fatty degeneration; scars are the result. But absorption is not possible in very old gummata lying in thick scar-like tissue; they may be partially calcified, but this seldom occurs to any degree.

A primary syphilitic epididymitis is very rare. The vas deferens is not usually involved, but it may undergo atrophy when the spermatic cord is compressed by scar and gummatous processes.

(*c*) **Leprosy.**—There occur changes in the testicles, particularly in the epididymis, which lead to atrophy of the testes and early—according to Babes even in the first year—impotence. Doutrelepont and Wolters found the testes coursed through by fibrous bands, and Babes, one of the most experienced investigators of leprosy, saw a productive interstitial inflammation in the beginning; he found the bacilli, at first, in larger plasma cells in the infiltrated walls of the tubules of the epididymis and the interstitial tissue of the testes, and later in large masses, (leprosy bodies), in the compressed seminiferous tubules. On the other hand, Simmonds, on the basis of two cases, believes that there is primary destruction of the seminiferous cells via hematogenous routes and excretion of the bacilli through the seminiferous tubules; after destruction of their cells the tubules disintegrate and secondary interstitial changes follow; the end result is a fibrosis of the small relaxed testis. Babes also speaks of hard, small testes. Simmonds saw a large increase in the number of interstitial cells (p. 1480).

(*d*) **Actinomycosis.**—Metastatic nodules in the testes are very rare. The collection at Basle contains a specimen with two nodules, one as large as a walnut, and one as large as a pea, (fig. 772), which were of yellow color and soft consistency.

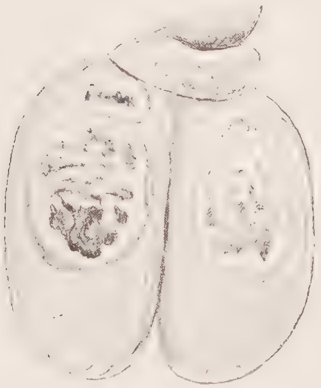


FIG. 772.—Actinomycosis of r. testicle (see text); metastatic in the case mentioned, p. 61 of actinomycosis of the organs of the neck, lungs, pericardium and heart. Fungi were found by Gram's staining.

Glanders.—In chronic glanders there are occasionally caseous-fibrous masses in the testes. Consult the general aspect and the histological processes under nose, p. 298.

Leukemic infiltration, diffuse or nodular, occurs in these organs as well as in others.

Cysts of the Testes.—Retention cysts in the testes or epididymis arising from stasis of secretion contain material mixed with spermatozoa (spermatocele, spermatocysts), or without spermatozoa, and consist of clear or milky fluid (galactoceles).

Spermatoceles are usually found in the head of the epididymis or in the rete testis. According to Virchow and Roth, these come from aberrant vasa of the Wolffian body, small passageways which have not been joined with the canal system of the epididymis or the rete testis, but remain in communication with them, and allow semen to backflow but not to empty. These sacs may reach the size of fists or more, and may appear in youth; as stated, they are usually in the head of the epididymis but if they arise from the rete testis, particularly in older men, they creep from the lower part of the rete to the epididymis toward the inguinal canal and reach to the turning point of the tunica vagina propria. Spermatoceles are usually lined with ciliated epithelium, but occasionally with a simple cylindrical or even with squamous epithelium. Cystic dilatation of Morgagni's hydatids of the epididymis containing spermatozoa may arise from an aberrant vas with a blind end in the hydatid dilated to a spermatocele (Roth). When the fluid in a hydrocele contains spermatozoa (spermatic hydrocele) they may have come from a spermatocele ruptured into the hydrocele, or a congenitally anomalous aberrant vas of the epididymis in the neighborhood of Morgagni's hydatid emptied freely into the cavity of the tunica vaginalis (Roth).

For cystoids, see p. 1504. Dermoid cysts are described on p. 1504.

Tumors of the Testes.—In general they are rare; they may occur in childhood. They show many different forms, particularly combinations of tumor tissue of various types which makes almost impossible classification into one of the ordinary histological groups. In the testes the chief tumors are solid, but many are cystic or small-cystic. The testis usually retains its egg-shape, even if enlarged; this is because of the tough albuginea.

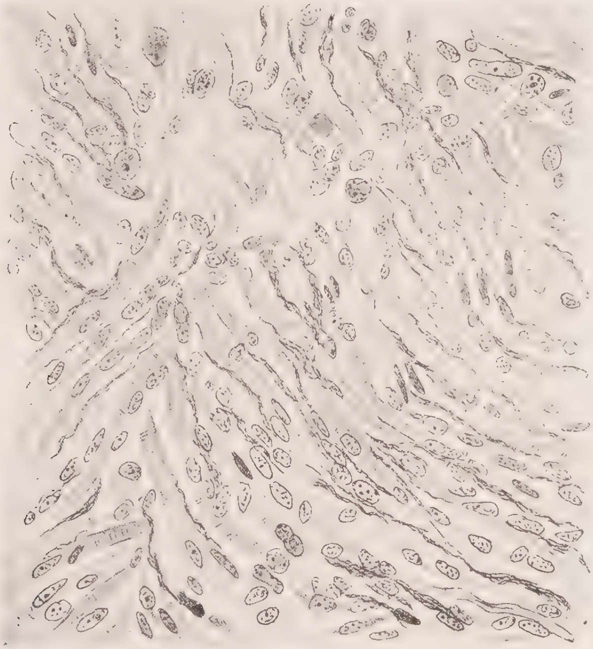


FIG. 773.—Malignant rhabdomyoma of testicle; boy 5 years old; details in text, p. 1496. (High power.)

Connective Tissue Tumors.—(1) **Fibromas,** occurring occasionally in the albuginea, and in the rete testis, and also in the epididymis, in the form of small nodules, are very rare. (2) **Lipomas** are occasionally found in the spermatic cord and epididymis (Wildbolz). (3) **Myxomas** are found combined with lipomas. These lobulated tumors are quite rare. On the other hand, myxomatous places are frequent in other tumors (adenomas, sarcomas). (4) **Pure myomas,** and myoma laevicellulare, (the author saw one as large as an almond in the epididymis of a 43 year old man), as well as rhabdomyomas, are fleshy tumors lying in (Neumann), or completely replacing the testis, (Arnold); they also are very rare. According to Benenati, the frequence of myxomas of the testes is one less than that of the same tumors of the kidneys. The author examined a solid malignant rhabdomyoma as large as a small fist from a 5 year old boy in whom the testis had been totally substituted by the tumor; on section it was quite similar in appearance to a juicy fibromyoma of the uterus; the extraordinary polymorphism of the fibers and cells justified the diagnosis of malignant rhabdomyoma. On the other hand, the presence of smooth or striped muscle fibers in other mixed tumors, particularly adeno-cysts, is not rare. But there also occur cystomyomas. Points of origin: the internal cremaster muscle, gubernaculum Hunteri, the muscle sheath of the epididymis, perhaps also erratic embryonal tissue (p. 1503). Many believe that rhabdomyomas are in reality mixed tumors in which only one particular tissue has grown. See Sakaguchi (lit.) concerning adeno-myomas of the epididymis. (5) **Pure enchondromas** are rare; their appearance is occasionally favored by trauma, or, at least, is preceded by trauma. According to their form, they are nodular or branched; they are capable of producing metastases in both regional lymph nodes and distant organs just as malignant tumors. Masses of branching or worm-like cartilage are frequently parts of a teratomatous mixed tumor; they often lie in lymph vessels or in seminiferous tubules. This is particularly frequent in the many-cystic teratomas (fig. 779), less common in carcinomas (lit. Mackenzie, Wallis), and sarcomas. Points of origin: connective tissue (Virchow), aberrant embryonal cartilage anlage (Billroth) snared at the time when the testes lie close to the vertebral column, the endothelium of lymph vessels (Paget, Wartmann); for the theory of Wilms, see p. 1504. (6) **Osteomas** are very rare.

(7) **Sarcomas.**—All sorts appear in children as well as in older individuals; many are mixed tumors. As a rule they first involve the testes, often bilaterally; they are less common than carcinomas; they vary from a soft medullary to a tough consistency, and infiltrate the entire testis and epididymis, or compromise the parenchyma to a small peripheral edge. Tumor masses invade the soft tissues of the spermatic cord. Less commonly, they rupture through the tunica albuginea and grow as sarcomatous fungi through the perforated skin. Rupture into blood and lymph vessels, and metastases, (see p. 1510), are more frequent in the medullary forms.

They occur much less frequently than carcinomas, and if the large cell tumor described on p. 1500 is accepted as a carcinoma, they are quite rare. In 32 malignant testicular tumors, Sakaguchi found one sarcoma; A. Vecchi (lit.) found two sarcomas among thirty-six.

In some, the section surface is uniform, fleshy and red white; in others, it is soft from fatty degeneration, necrosis often plainly due to thrombosis of vessels, hemorrhages, mucoid softening and calcification. The various kinds of sarcomas are: round cell, which may appear as congenital tumors, particularly prone to regressive changes, and therefore quite soft; occasionally the section surface is entirely homogeneous, glassy, pale white red, and the testes and epididymis have disappeared. In Breslau, the author performed an autopsy on a 3 year old child with an uncommon case of round cell sarcoma. The right testis, as large as a hen's egg and of egg shape, was replaced entirely by white, moderately firm, smooth, glassy tumor tissue at the internal inguinal ring; upwards from this there was a nodule as large as a child's fist. An interesting feature of the case was the fact that in the right half of the scrotum, there was a nodule as large as a goose egg, which gave the impression of a primary tumor invading the spermatic cord, and which was removed with the clinical diagnosis of sarcoma. The left testis was intact.

Spindle cell sarcomas are usually hard, often lobulated, may contain giant cells and cross striated muscle fibers; the author saw such a tumor in the epididymis of a two year old boy; occasionally there occur fibrosarcomas, perhaps arranged in perivascular fashion (perivascular or plexiform angiosarcoma). (Fig. on p. 1212.) Moist, fairly soft myxosarcomas and pigment sarcomas also occur. Even combinations of sarcomas and carcinomas have been described. In many sarcomas there are spaces cystic from mucoid softening; in others of teratoid nature the cysts are dilatations of epithelial-lined tubules (cystosarcomas). Nodular tumor masses may grow into the tubules and stretch them (intracanalicular sarcoma), but usually only in isolated places in otherwise solid tumors. Many sarcomas contain glycogen (Langhans). Occasionally the differentiation of sarcoma from carcinoma is very difficult. Krompecher believes that endotheliomas (lymphangio-endotheliomas) of alveolar structure are the most frequent malignant tumors of the testes. The author cannot subscribe to this statement; these large cell tumors are of epithelial nature, *i.e.*, solid carcinomas (see the work of Sakaguchi who found 23 large cell epithelial tumors among 32 testicular tumors). See p. 1504 for the theories of their genesis.

Interstitial cell tumors are discussed on p. 1481.

Epithelial Tumors

Adenomas occur in children as well as adults as glandular solid nodules similar in structure to the tubules of the organ.

Pure tubular adenomas are very rare. They have been described as multiple, white to butter-yellow, round cornered nodules in ectopic testes and in masculine pseudohermaphroditism (Pick, the author, Lecene and Chevassu); their development from Sertoli's cells of preexisting seminiferous tubules was proved quite definitely. See R. Meyer concerning adenomas of the rete testis.

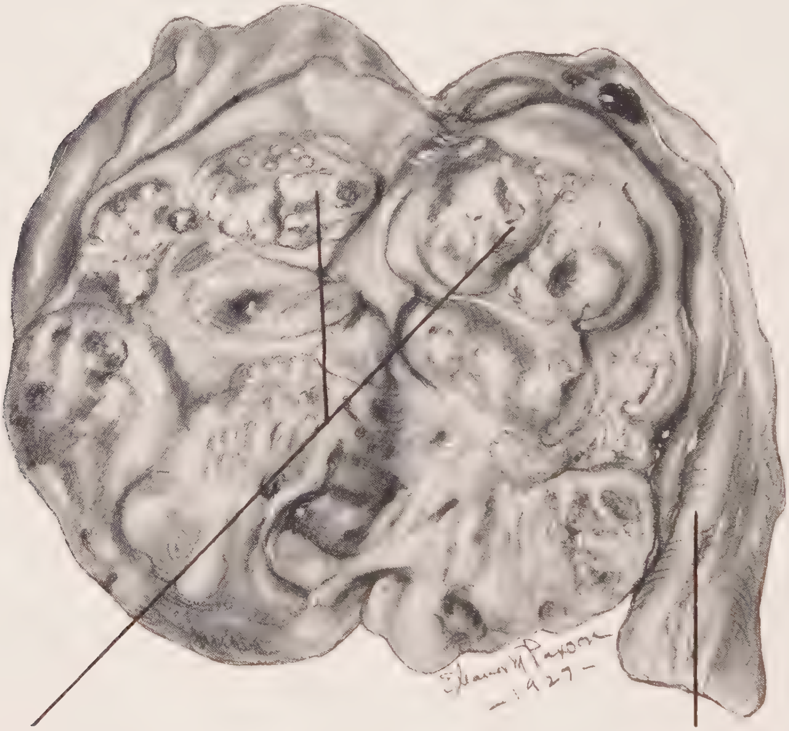


Fig. 774.—Adenocarcinoma of the right testis. Testis split longitudinally to show a number of nodules which bulged on the surface and were comparatively soft and juicy, yellow gray in color and cellular. Microscopically the epithelial cells formed typical gland structures with lumena in their centers. L. H. #779. ⅜ nat. size.

It has not been definitely proved that adenomas in ectopic testes can become carcinomas, but the possibility is present (Uffreduzzi).

Carcinomas.—Their macroscopic appearance is quite varied. The solid forms (*a*) are usually soft in consistency, but may be quite firm; tumor juice may be squeezed from the section surfaces, which then appear cloudy, yellow-white, medullary, here and there somewhat nodular; the section surface of other tumors is glassy, pale-gray, without architecture but quite moist. They are quite similar to many sarcomas. As carcinomas undergo degeneration through fatty or mucoid changes, or as hemorrhages or necroses set in, the section surface becomes variegated. Many soft carcinomas are telangiectatic. While most testes containing soft carcinomas are very voluminous, there also occur hard, dense, scirrhous varieties without particular enlargement of the testis. Cystocarcinomas (*b*) are macroscopically similar to the many-cystic teratoids (so-called adenocystomas), but the former always eventually involve the epididymis, while in the latter the epididymis remains free (see A. Vecchi). The tunica albuginea and the egg-shape of the testicle are usually retained for a long time. The light rose-colored albuginea is traversed by broad tortuous veins. Rupture through the albuginea and the tunica vaginalis or the skin of the scrotum is very rare. Carcinomas arising from the epididymis are rare.

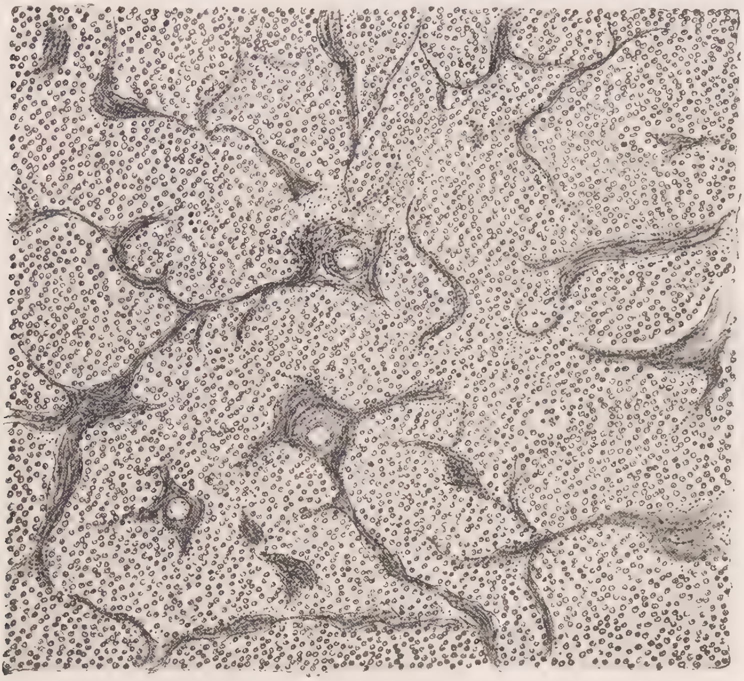


Fig. 775.—Carcinoma of testicle. Rounded polymorphous large epith. cells in large groups; in between fibrous interstitial tissue showing marked small cell infiltration and some vessels; L. testicle 1170 gms., from man 50 years old. On sect. pale yellow, caseous, friable except a few glassy pale gray red places. (Medium magn.)

Sakaguchi, in his case, believes the point of origin was the epithelium of the tubules of the epididymis.

Carcinomas of the testes are most frequent in the fourth decade; they do appear in the second and third decade; from the sixth decade onward they are quite rare. According to the statistics of Chevassu, there occurred 41 cases from 20 to 40 years, 10 cases previous, 15 from 41 to 50, and only 3 after 50 years of age. In 13 observations of the author, 3 occurred in the third decade, 5 in the fourth; the others occurred in the fifth decade (1 case), in the sixth (2), in the seventh and eighth (1 case in each); the oldest individual was 75 years of age. The large cell epithelial tumors prefer the younger men; adeno-carcinomas are found in childhood as well as in extreme old age (compare Sakaguchi).

Histological. Some are pure carcinomas, others belong to the mixed tumors. According to Langhans, the former originate from the germinal cells of the seminiferous tubules, or from the cells of the spermatogonia, a view which is shared by many; but Langhans himself later recommended a re-examination of this question. Ribbert believes it is impossible for them to originate from cells of seminiferous tubules; he thinks rather that they are embryomas, coming from early germinal cells, of an age close to that of the segmentation stage. Thus carcinomas originate indirectly from the germinal cells of the testis, even though not from those of the finished organ, but from their first anlage; the other

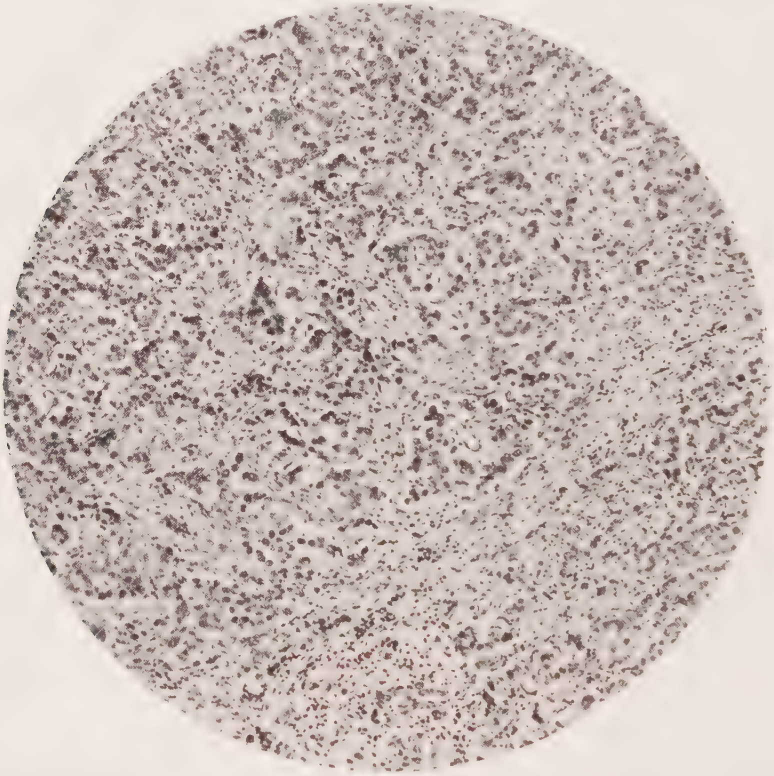


Fig. 776.—Carcinoma of the testis from a man 28 years old. The cells are smaller than in fig. 777, more loosely arranged in alveoli and do not tend to form definite structures. Therefore the diagnosis of large cell sarcoma is readily made unless other features are taken into consideration. L. H. #559.

parts of an embryoma such as cartilage, bone, etc., need not be found when the carcinoma spreads diffusely (compare B. Fischer, Uffreduzzi). A. Vecchi (lit.) believes this is possible in certain cases; therefore, they are mixed tumors of carcinomatous type, in which the epithelial component gains the upper hand; among his 24 cases, Vecchi found ciliated epithelial cysts and bones in a few; the great majority, however, he considered simple tumors, which originated from an overgrowth of the embryonal or the adult seminiferous epithelium. The most common are (*a*) simple solid carcinomas or medullary carcinomas, the so-called large cell testicular tumors, usually beginning as nodules in the center of the testis, but growing rapidly and diffusely through both testis and epididymis, so that, with the exception of a stroma rich in round cells, the actual parenchyma of these organs is reduced to small remnants. The entire tissue mass consists of large rounded or polyhedral cells gathered together in indistinct alveoli, cells which are quite sensitive to the ordinary fixing fluid so that shrinkage

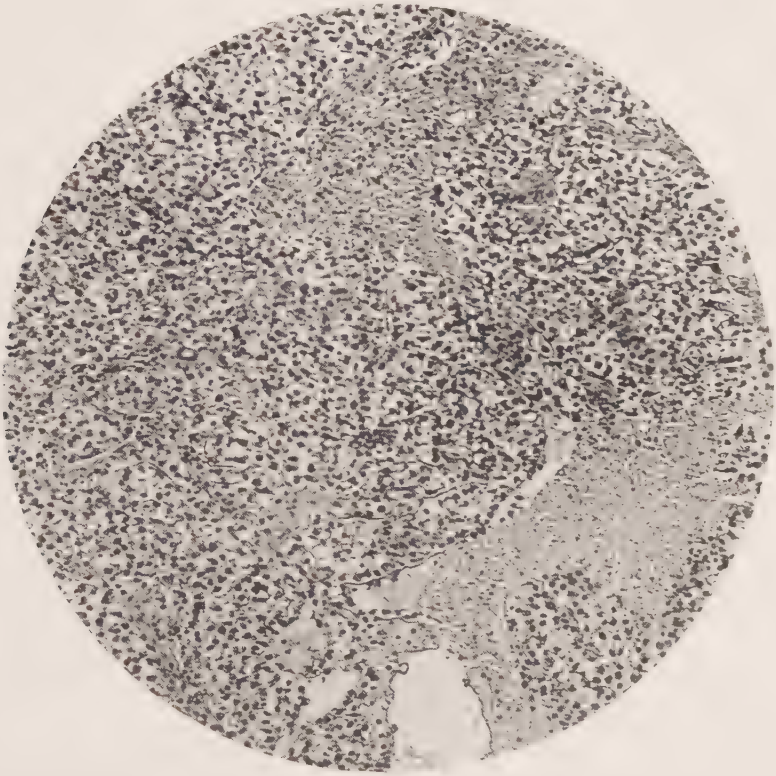


FIG. 777.—Carcinoma of the testis from a man 28 years old. This was noticed shortly after trauma, as many of them are, but the exact relationship is, of course, **sub judice.** The cells in this case are quite large and are attached to each other in strands with here and there an attempt at an imitation of a duct or acini. The diagnosis of carcinoma is therefore not so difficult in this case as in fig. 776. L. H.

brings out the interstitial substance and leads to mistakes with large cell sarcomas. They are almost always rich in glycogen. Since, as stated, these large cell testicular malignant tumors were formerly mistaken for sarcomas or endotheliomas, their carcinomatous nature has been distinctly emphasized by Chevassu who speaks of "seminoma," (see also Chenot), by Debernardi who speaks of large cell tumors, by Albrecht, Conforti, A. Vecchi, Frank, Sakaguchi (lit.), and by Ewing who speak of embryonal carcinoma. (*b*) The adenocarcinomas are much less common, but are occasionally mixed in with solid parts, and are frequently of delicate arcade-like or papillary structure. This architecture also appears in the metastases which frequently reach extraordinary size, particularly those in the abdominal lymph nodes and in the liver; in a 26 year old student, the author saw a moderate increase of temperature, numerous scarlatinal hemorrhages into the skin, and a fatal hemorrhage from a nodule in the liver. It is thought that they arise from the tubuli recti or the rete tubules, derivative of the sexual part of the Wolffian body (A. Vecchi, Sakaguchi); perhaps, however, they may arise from indifferent predecessors also. Origin from an adenoma is possible. Both forms, (*a*) and (*b*),

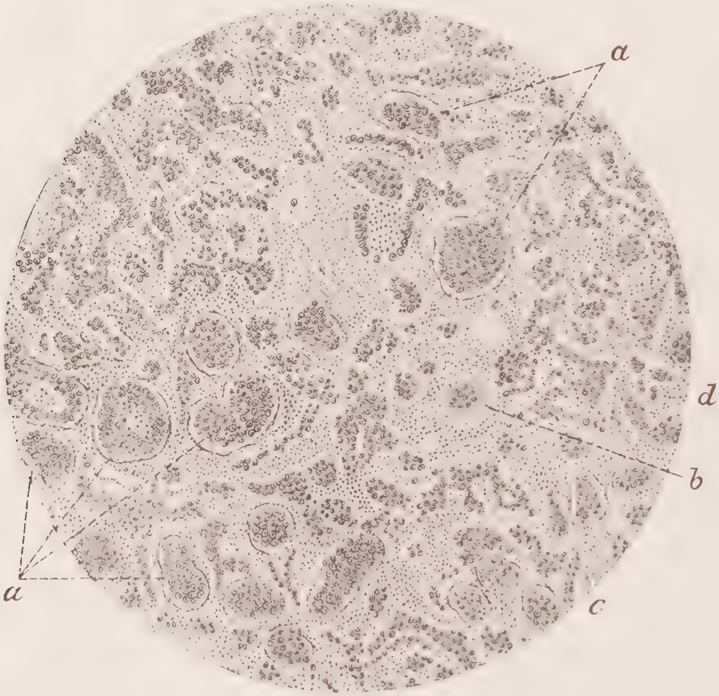


FIG. 778.—Large cell carcinoma of testicle with small alveolar structure; a, seminiferous tubule meshes filled with tumor cells; b, atrophic tubule; c, hyalin capillary; d, lymphocytic infiltration; tumor of undescended testicle (in inguin. canal) of man 35 years old. (Pub. by Sakaguchi.) (Med. magn.)

occur in abdominal testes (Espersen and lit. p. 1476). (*c*) Scirrhous solid carcinomas are less common; they have a tendency to infiltrating growth of a uniform delicate microscopic picture, inasmuch as the strands grow into the smallest tissue spaces and anastomose with each other; the islands may be surrounded by thin hyalinized homogeneous septa. The normal tissue may disappear completely. In mixed tumors as well as teratoids (see below) a very neat adeno-carcinomatous structure is common. Colloid carcinomas are very rare. Rowlands and Nicholson have described a squamous epithelioma of the epididymis. (Ribbert believes that it was probably an embryoma.)

In mixed tumors various combinations appear of carcinoma with adenocystoma and with sarcoma (see p. 1504, theory of Wilms, also see under ovaries). Albrecht described sarcocarcinomas, tumors which, in their largest part, consist of carcinoma of one of the above mentioned types; the interstitial tissue is, however, sarcomatous and produces syncytium-like pictures; the metastases are often hemorrhagic.

See p. 1506 concerning metastases.

Dermoid Cysts and Teratomas.—Simple dermoid cysts of the testis containing all of the attributes of the epidermis or the entire skin (sebaceous glands, hair; see de Vecchi) are relatively rare, particularly as compared to their incidence in the ovary. Complex dermoid cysts are likewise rare; by these are meant mixed tumors in which a cystic sac is the principal structure as in the ovaries, and, in principle, in other parts of the body; their ectodermal part is often of least importance. In the mixed tumors of the ovary, however, there are usually found skin and hair which justify the term "dermoid." Solid teratomas (*i.e.*, tumors containing small and many cysts, or those which macroscopically are mostly or entirely solid) are mixed tumors composed of many kinds of tissue, and are more frequent in the testes than in the ovaries. Macroscopically, they may appear merely medullary, and their complicated structure and their many cysts are first detected on microscopic examination. The teratomatous mixed tumors of the testes met in children as well as in adults, but usually not after the fortieth year of life, are more frequent in the right testis (Ohkubo); rarely they are bilateral (Sakaguchi, lit.).

Malignant teratomas likewise occur in relatively young individuals.

The origin of teratomas has stimulated many theories. While Klebs believes they originate from misplaced germinal cells, the theory of Wilms, which is particularly well worked out for ovarian teratomas (see under these tumors), states that the teratomas of both the testes and ovaries are products of a germinal anlage consisting of three layers, which have come from a sex cell (in this case a spermatic cell) which had developed parthenogenetically. In one case (dermoid cysts—rudimentary parasites

—embryoma), these three layered germinal anlage lead to the formation of the rudiment of a foetus in the form of a "head nodule," *i.e.*, a wart-like protuberance in the seeming dermoid cyst, which, histologically is found to be made up of extraordinarily varied tissues. In this rudimentary structure, *i.e.*, in the dermoid cyst, the growth reaches a certain degree of differentiation, while in the embryoid tumors—solid teratomas, teratoids, now also called embryonal teratomas or teratoblastomas, the embryonal tissue reaches a certain degree of differentiation without the formation of organ parts; it grows further without bounds or design. The term "solid" is used merely in contrast to the term "cystic" in the sense of a cystic sac as found in dermoid cysts; the many-cystic teratoids, formerly called adenocystomas, are considered by Wilms to belong to the "solid" teratomas. In both cases, according to Wilms, as a rule, only those tissues grow in the tumors which normally are developed earliest, *i.e.*, the ectoderm, and particularly the upper parts of the body. These in their further growth choke off the other tissues, or the latter disappear for other reasons.

Furthermore, according to Wilms, the solid embryoid tumors (teratoids) include the predominantly solid mixed tumors, as well as those which contain many cysts and which were formerly called cystoids, and those which consist almost exclusively of innumerable cysts lined by cylindrical ciliated, or squamous epithelium; these two latter are composed of glandular structures, cartilage, smooth or striped muscle, etc., one or another part of which is more markedly developed; furthermore they may also have carcinomatous components. Names proposed are therefore cystochondromyomas, cystomyomas, cystocarcinomas, etc., according to their composition. Finally, these different structures are possible because the germinal layer grows not merely as a whole, but isolated tissues of these germinal layers take on a dominating strength, so that other parts are overgrown (Wilms). Thus a tumor may be the product of only two germinal layers ("bidermoma" Wilms, teratoma biphyllicum), or of only one *e.g.*, cartilage or muscle, but in many such cases a complete examination shows other products. This theory of Wilms has been very fruitful in tumors (Ribbert), even though it probably goes too far (compare Risel) when pushed to its final conclusion, viz., that every tumor arises in this manner. And although one part of the theory, viz., the assumption of parthenogenetic development from a sex cell, has been shown to be erroneous, and has been abandoned by Wilms in favor of the blastomere hypothesis of Marchand-Bonnet (see under ovaries, p. 1586), nevertheless the demonstration merely of the complex structure of these tumors has been very valuable; it at least emphasizes the idea that the point of origin being a sex cell, more or less equal differentiation is possible from either spermatozoan or ovum. (For more details, see under embryomas of the ovary, p. 1583, and compare R. Meyer.)

As stated, the many-cystic teratoids were formerly called adenocystomas or cystoids, or cystadenomas, or multilocular cystomas. The cysts themselves may be small and grouped thickly together, whereupon the tumor is often accompanied by considerable enlargement of the testis; in other cases—the more frequent—larger cysts dominate the picture so completely that it is only a microscopic examination which recognizes the varied tissues between the cysts; occasionally other tissue types, particularly cartilage, can be seen grossly in larger masses between the cysts (fig. 779). The cysts contain mucoid spermatozoa-free fluid and are generally lined with simple or stratified cylindrical, goblet or ciliated epithelium; others contain yellow white atheromatous masses and are

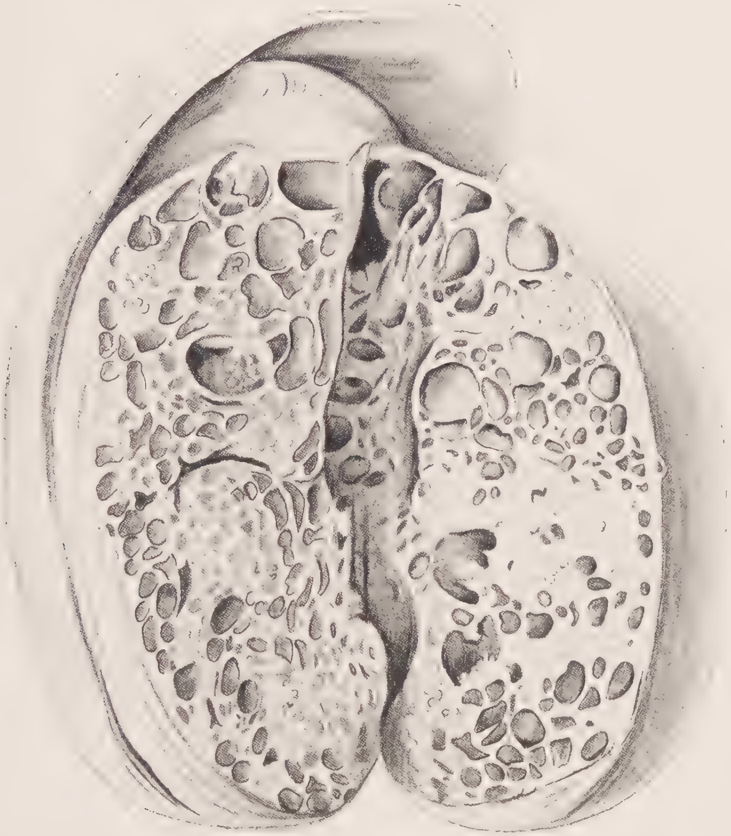


Fig. 779.—Teratomatous mixed tumor (teratoid) of testicle, multiple cyst formation; varying epithelial lining; some epidermoidal; contents of cysts partly gelatinous, partly mushy; also contained cartilage. Microscopically demonstrable strands of smooth muscle (embryoid tumor in Wilm's sense, formerly so-called cystoid); epididymis free. Operative spec.; ¾ nat. size.

lined by many layers of epithelium of an epidermoid character (the so-called atheromatous cystadenoma, Langhans-Kocher).

The microscopic examination of these many-cystic teratomas (teratoblastomas) shows that derivatives of all three germinal layers are present. Goblet, cylindrical, and ciliated cells arise from the entoderm, and not only line the grossly visible cysts, but also form gland-like structures similar to the glands in the digestive and respiratory apparatus; connective tissue, cartilage, bone, smooth and striped muscle, vessels, come from the mesoderm; epidermoid cysts, as well as the not uncommon tissues resembling the nervous system, such as neuro-epithelium, plexus-like formations, and pigment cells, come from the ectoderm. From the latter also arise most of the chorion epitheliomatous structures (see below), occasionally present. Cartilage is usually present in considerable quantities; cross striated muscle, and nervous tissue, among others, may be completely lacking. The older views concerning the so-called cystoids state that they are related to Wolffian bodies, or to misplaced embryonal tissues in the testes, (see, among others, Recklinghausen, Langhans-Huguenin, Cavazzani; see opposed, R. Meyer); Debernardi agrees in a number of embryoid tumors, or teratoids in the sense of Wilms (p. 1504). But if he believes this true of some of the cases, and not in others with the evident structure of adenomas, and believes they are simple mesodermal mixed tumors, he cannot possibly be correct, since derivatives of all three germinal layers can be found almost constantly.

The microscopic examination of solid or almost solid teratomas (teratoblastomas) leads to the discovery of derivatives of all three germinal layers (teratoblastoma triphyllicum), or to more or less domination of one layer, or to only isolated tissues of one germinal layer, while the other parts are outgrown. (Consult p. 1504.)

Course. -Teratoids of the testes usually grow slowly and remain benign in spite of considerable size. Occasionally in both solid and cystic teratoblastomas, a carcinomatous (usually adenocarcinomatous) or sarcomatous part appears determinable only by the microscope. Care must always be exercised in the prognosis, particularly in harmless appearing, many-cystic teratomas. Growth of the primary tumor may become vigorous but is not necessary; extensive metastases have occurred when the primary tumor was quite small. The metastases may contain all of the components of the primary tumor, or, as a rule, (compare the work of Mori, lit.), only one or another part which is predominant in the primary tumor. When the metastases are of a particular type, *e.g.*, an adenocarcinoma, this type can usually be found here and there in the primary tumor. For exceptions, see under chorion epitheliomatous teratoids, p. 1507.

Occasionally, descriptions have appeared of chorion epitheliomatous and hydatidiform mole-like structures in teratomas of the testes (see under uterus and under teratomas of the ovaries, p. 1588); (Schlagenhaufer, Carey and others, Risel, lit., Chevassu, Orton, Chuvin). They are believed to arise from the ectodermal part (fetal ectoderm) of the teratoma. We have mentioned their occurrence in the so-called cystoids on p. 1506, in which their mass is usually unimportant; in some cases they comprise a large part of the tumor, while in still others they are predominant. When metastasis is wide spread the chorion epitheliomatous structures appear in the secondary growths, as in the cases of Schlagenhaufer, Emanuel, W. Fischer (abdominal testis); in Glaserfeld's case the teratomatous testicular tumor showed only sparse syncytia; in the cases of Fritze and of Stark, lit., (teratoma triphyllicum as large as a cherry), it showed none, but the metastases were composed of typical chorionepithelioma. Lit. by Conforti, Mori, Fuglistaller, van Ryssel, Langer, Comen, Joh. Volkmann.

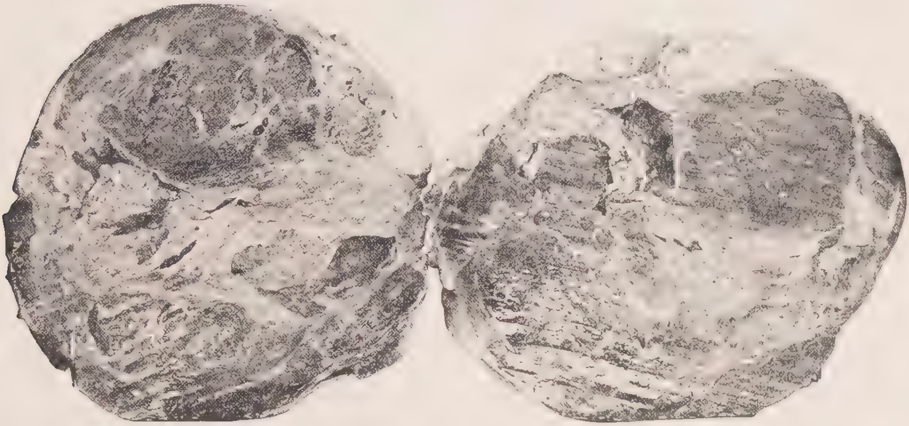


FIG. 780.—Tumor of testicle containing chorionepithelioma, described in text below; man 43 years old; see fig. 781; not quite ¾ nat. size.

Occasionally there occur (probably) entirely pure chorion epithelioma-like tumors without other teratomatous parts, as in the cases of Fink, Scott-Longcope, (abdominal testis), Frank, Oberndorfer-Seckel-Sigl, Zenoni, Reckendorf, (abdominal testis). It must then be supposed that the original tumor was an early three germinal layer teratoma in which the chorion-epitheliomatous parts finally totally overgrew the others (Pick). The following observation is along these lines: after examining a large number of sections, the author came to the conclusion, in the case illustrated, fig. 780, that it was a "pure" chorion-epithelioma. A later, very careful, examination by Determann showed, however, that this tumor contained parts from all three germinal layers, particularly a large amount of central nervous tissue (see also I. Diss. C. Hoernicke). Finally, Hartmann and Peyron also emphasized the addition of other tissues of a teratoma to the chorion epitheliomatous parts. This case was in a 43 year old man, the father of ten children; the testis weighed 670 grams, and was composed almost exclusively of chorion-epithelioma. The tumor (figs. 780 and 781) is said to have appeared one year after trauma. Death occurred one month after removal of the testis; metastases were found in the retroperitoneal lymph nodes, the left kidney and in the lungs, all of a chorion-epitheliomatous structure. On section, the tumor was found to be panelled; it showed a striking mixture of hemorrhagic, discolored, caseous, necrotic, with well preserved, finely granular, spongy, light gray portions somewhat similar to placental tissue. The epididymis was not involved. This structure was also found in the metastases and was characterized by hemorrhages and extensive necrosis from the destruction of vessels by tumor cells just as in the chorion epithelioma of the woman. The microscopic picture is quite clear, quite uniform in many situations, and so similar to the chorion epithelioma of the woman, that even the fine ciliated

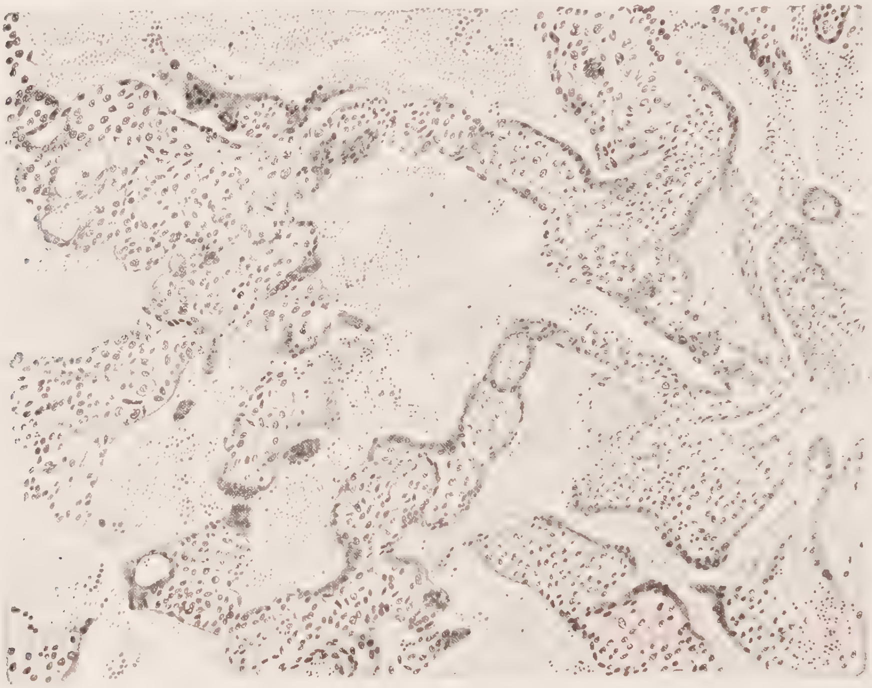


Fig. 781.—Chorionepitheliomatous tumor of testicle; strands and columns lighter cells (Langhan's) and dark stained syncytium with nuclei rich in chromatin; the syncytium often forms giant cell-like structures. Between the columns blood, fibrinous coagulum, and (outward to right) thrombi. Man 43 years old; mentioned above. (Med. magn.)

border, like that of an hydatidiform mole, was found in the syncytia of the primary tumor and in the metastases.

In a testis removed because of "teratoma chorioectodermale," Hedinger found overgrowth of the interstitial cells in the other testis, but Berblinger in his case could not find the same occurrence.

Finally, it must be mentioned in these mixed tumors of the testes, and in single layer tumor forms with chorion epitheliomatous growths, particularly syncytia, that many authors believe them sarcomatous from perithelium and endothelium of blood and lymph channels (Malassez and Monod and others, C. Sternberg, Monckeberg, lit.), or merely as sarcomas with richly developed primitive blood capillaries (Goldzieher), at any rate, as of connective tissue origin (H. Albrecht). The syncytia probably do not originate from one source (compare Herzog, H. Sternberg), but even the one case in which the author found the ciliated border on the syncytia, speaks for the morphologic similarity to the chorion epithelioma of the woman. In two cases, Hartmann and Peyron observed the other signs of pregnancy, as proof of the specificity of this tumor, viz., hypertrophy of the breasts and secretion of colostrum. Furthermore, according to Hartmann and Peyron, the various testicular tumors of embryonal origin and increasing complexity represent the orderly progression of embryonal stages of the ovum, the embryo (in the strict sense of the word), and the fetus; when the trophoblast in these tumors, *i.e.*, the cells which normally bring about the union between the embryo and the mother, undergo proliferation, there arise "choriomas," in which the cells retain the character of the primitive chorionic ectoderm, and "placentomas," when higher developed stages of the placenta are reached. As stated (p. 1507), other parts of a teratoma are also found in these tumors. Compare the theory of L. Loeb concerning the parthenogenetic genesis of chorion epitheliomas, as discussed under ovarian teratomas. Recently Heijl tried to relate the chorion epitheliomatous structure with central nervous tissue because Risel had observed the transition of neuro-epithelium into syncytia. Schlagenhaufer, on the other hand, believes it is the product of trophoblast, and thus the discovery of transition of neuro-epithelium into syncytia is of no importance; he believes the ectodermal genesis is uncertain, the more so since a close relationship between the trophoblast and the ectoderm is not generally recognized (see Mewes). In addition, an ectodermal genesis is difficult to understand if we remember that ovarian teratomas usually contain much ectoderm, but chorion epitheliomatous structures are amongst the greatest of rarities, while in the testes the reverse is the case. See also Kaiserling.

All malignant testicular tumors are alike in that the metastases occasionally are enormous in comparison to the primary tumors; this is particularly true of secondary growths in the retroperitoneal (ileo lumbar) lymph nodes, perhaps larger than a man's head (see Staffeld and compare Zausch); finally the veins (of the spermatic cord, inferior cava), the liver and the lungs are particularly favored (consult Mori). As Chevassu emphasizes, however, early removal of the primary growth yields a good chance for recovery, because local recurrence is delayed in the tough albuginea, and the sharp boundaries of retroperitoneal lymph nodes make their removal easier. But the author's experience indicates a poor prognosis (compare Mori), especially with those which metastasize into almost all the organs, even the brain, by way of the blood channels, and which are predominantly (or entirely?) chorion epitheliomatous. Morris emphasizes that the cylindrical cell carcinomas of the testes tend to recurrences in the lymph nodes even though late.

Secondary metastatic tumors are occasionally observed in the testes or the epididymis, both from carcinomas, and, more frequently, from sarcomas, particularly the melanotic variety.

See the appendix for literature concerning testicular tumors.

Parasites.—The occurrence of echinococcus in the testes, epididymis or in the tunica vaginalis may be mentioned, (very rare).

Atrophy of the Testes. Hypertrophy.—In old age, the testes become smaller, softer, browner (p. 1480), or, on the contrary, harder and richer in connective tissue. The former may be called "the normal senile testis," (Spangaros). Spermatogenesis may be retained, but the tubules are narrow, their cells are pressed together, the walls are thickened by increase of elastic tissue under the hyalin layer. The other form is more severe, the spermatogonia lose their reproductive power, finally disappear via granular destruction and fatty degeneration, Sertoli's cells disappear later and the lumena of the thick walled tubules lie close together as small spaces (Spangaro). Thus the picture is quite similar to spermatoangitis fibrosa obliterans (Eug. Fraenkel, p. 1486), and it is quite difficult to differentiate what etiology is responsible for one or the other of the fibrous spots in the senile testis. But atrophy of the testes does occur in younger individuals from causes as stated on p. 1480 (see also Goette), *i.e.*, in cachexia and central nervous diseases; small, soft, uniformly dark brown or dark brown spotted white or gray-red testes are found. In bronze diabetes the testes contain large masses of iron-containing pigment both in the connective tissue and epithelial cells. If no spermatozoa are produced, the condition is called azoospermia. The production of spermatozoa may cease temporarily during acute illnesses (Cordes). There is considerable variation as to the age at which the reproductive abilities of the spermatogonia (senile involution of the testes), the sexual potence and the libido, cease; the latter, however, is not entirely dependent upon a functioning sex gland (p. 1186). Many men 80 years old, and even 90, still produce spermatozoa (Demange). Wegelin describes a spermiophagia, *i.e.*, a phagocytosis of spermatozoa by desquamated epithelial cells, large and rounded, about 15 to 40 microns in diameter containing the heads of spermatozoa in their large vesicular nuclei. It becomes more marked about the fiftieth year of life, and after the seventieth year is an almost constant finding; at the height of manhood, it is rare. Chronic diseases, alcoholism, phthisis, favor this process. Simmonds and Bertholet state that in alcoholism, notoriously followed by disappearance of spermatogenesis and loss of potentia generandi, the testes need not be macroscopically diseased, but that microscopically, the essential changes are thickening and hyalin changes in the semeniferous tubule walls, metamorphosis of spermatogonia into cylindrical or cubical epithelial cells and narrowing of the lumena of the tubules. According to Weichselbaum and Kyrle, chronic alcoholism may lead to complete destruction of the semeniferous tubules; well marked overgrowth of the interstitial cells and the epithelium of the rete testis appears, the latter as a sort of fruitless regeneration. Experimental observations in rabbits confirm these findings (Kyrle and Schopper, lit.). The atrophy following inflammation of the parenchyma and obstruction of the spermatic cord or induration of the epididymis has been described on pages 594 and 1484. Atrophy of the testes with destruction of tubules may also be caused by pressure of hydroceles (mild atrophy), hematoceles, hernias, tumors, etc. Retained testes and those surgically replaced always become atrophic very early (Stilling). For the retention of the interstitial cells in this condition, see p. 1480. If one testis is destroyed in a youthful individual, the other may enlarge by way of compensation. According to experiments by Ribbert, compensatory hypertrophy takes place chiefly along the lines of increased diameter of the semeniferous tubules.

Diseases of the Tunica Vaginalis and the Spermatic Cord.—Inflammations of the tunica vaginalis propria, vaginitis testis, vaginalitis or periorchitis occur primarily following traumata or from unknown causes, or secondarily following diseases of the testis and epididymis, and occasionally by the hematogenous route in septic conditions.

In **hydrocele,** or vaginitis serosa, the sac of the tunica vaginalis propria contains a serous or serofibrinous fluid. According to whether the processus vaginalis is open throughout its entire length, or open merely in the region of the spermatic cord, there appears from inflammatory exudation, a hydrocele processus vaginalis congenita or a hydrocele funiculi spermatici, which may be intra- or extra-inguinal in position. The processes in both cases may be open or closed toward the peritoneal cavity.

When a hernia is present in the open processus, serous inflammation produces a hydrocele herniosa.

Development.—Vaginitis serosa occurs in the newborn; it is usually insidious, but may appear acutely following contusions, or gonorrheal epididymitis. See p. 594 concerning hematogeneous vaginitis in mumps.

The so-called hydrocele muliebris is a collection of fluid in the processus vaginalis peritonei or the so-called canal of Nuck (compare Sellheim), which remained open from early embryonal life or closed later in the region of the external inguinal ring. The round ligaments form the posterior or lateral boundaries of the seeming cystic tumor in the region of the inguinal ring or the upper part of the labium majora; it may appear quite suddenly and give the clinical appearance of an irreducible inguinal hernia (Abel).

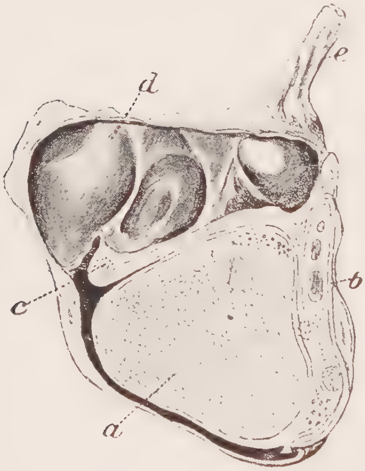


FIG. 782.—Cystic hydrocele of spermatic cord; hardened in chromic acid; a, testis with tunica vaginalis; b, epididymis; c, head of epididymis; d, cyst with projecting ridges; e, spermatic cord; nat. size.

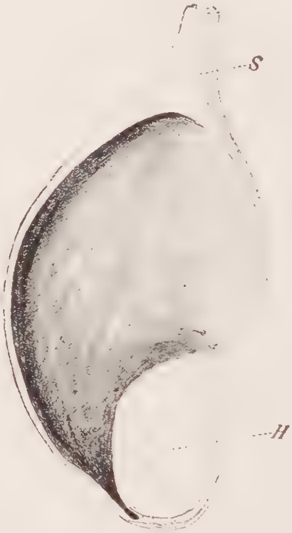


FIG. 783.—Hydrocele of tunica vaginalis propria; testis hardened in chromic acid; H, complete testis below backward; s, spermatic cord; $\frac{2}{3}$ nat. size.

In acute cases the fluid is clear, serous or mixed with pus cells and blood corpuscles. In chronic hydroceles, following the acute condition, or of insidious onset, the fluid may measure several liters; it usually is of high specific gravity, clear, yellow, albuminous, rich in fibrinogen, and contains a few leucocytes. Small fibrin flocculi contained in the fluid may be precipitated to the surface of the tunica vaginalis and lead to thready adhesions of the leaves. Frequently the fluid in an old large sac is bloody.

red or brown and contains cholesterin crystals. See p. 1494 for hydrocele spermatica.

The sac of a hydrocele tunica vaginalis usually takes the shape of a pear; the length of the pedicle up along the spermatic cord depends on the degree of opening of the processus vaginalis. The entire testicle is pushed to the posterior lower side of the sac, *i.e.*, toward the base of the scrotum, to which it is attached posteriorly where it is not covered by serosa. The testis itself, covered by scar tissue, becomes softened, and occasionally somewhat fibrous. Even when the hydrocele is as big as a fist or a man's head and contains many liters of fluid, the testis is not changed microscopically, except for a few foci of atrophic semeniferous tubules. The pressure atrophy, therefore, is not very marked.

In the hydrocele of sucklings and young children in whom chronic hydroceles are very frequent, the testis usually lies to the posterior upper side of the sac (W. H. Schultze).

The sacs of older hydroceles are thick, leathery, and the inner surface covered with irregular, fibrous, cartilaginous or calcareous plates (periorchitis plastica), with necrotic or atheromatous spots. Occasionally villous growths, (periorchitis prolifera), as in proliferating synovitis, lead to hyalin—cartilaginous free bodies, occasionally the size of cherries (Glass). In the tunica vaginalis in a case of old irreplaceable scrotal hernia, Sultan saw thousands of rice bodies without a drop of fluid; most of them were rounded, soft and compressible, as large as peas; their origin was said to be fibrinous degeneration of the thickened membrane with added growths of the endothelium of the wall and desquamated cells in agglutinated clumps. When adhesions are present (periorchitis adhaesiva), the hydrocele becomes multilocular.

Hematoceles.—They may arise (1) secondarily in a hydrocele following traumata, or spontaneously when an older sac is very vascular from inflammation. A hematocele funiculi spermatici may likewise arise from a hydrocele. Its contents become red or brown or yellow-brown; the size may be that of a man's head. Occasionally the wall is like that of an old aneurysmal sac, thick, hard, calcified, and covered by fibrin masses in layers. Through regressive changes, the contents become brown yellow or chocolate colored, fatty, rich in cholesterin or pigment. (2) A hematocele may follow trauma, or occur in the hemorrhagic diatheses independent of a hydrocele. These latter might be called hemorrhages into the unchanged cavity of the tunica vaginalis or hematomas of the tunica vaginalis. The fluid and clots remain for a long time. Later the coagula initiate an inflammation in the sac and the tumor is exactly like a typical hematocele. (3) Hemorrhages into the spermatic cord are called hematoma funiculi spermatici and are particularly voluminous when there is a varicocele. The latter are varicose dilatations of the veins in the spermatic cord which may extend into the testes and epididymis. Through the skin of the scrotum they are felt as convoluted vermicular strands; the walls of the veins become thickened. They are more frequent on the left side because the left spermatic vein empties at right angles into the left renal vein, and stasis is more likely to occur there than in the right spermatic vein, which empties directly into the inferior vena cava. Others believe the explanation lies in the fact that the left testis usually hangs lower than the right, and that the scrotum is carried in the left leg of the trousers; Konig saw right-sided varicoceles in those who carry the scrotum in the right leg of the trousers. Functional disturbances and atrophic changes in the testes are rare in this condition. Spontaneous regression often takes place in old age (Konig). Even hydroceles may be developed through stasis, *i.e.*, hindrance to the outflow of blood from the pressure of tumors, hernias, etc., but usually the causes, apart from the anatomical conditions mentioned, are unknown.

Intravaginal hematoceles, in contrast to extravaginal hematoceles, are also described; the latter are hemorrhages into the soft tissues of the scrotum, a condition also termed hematoma scroti.

Vaginitis or periorchitis purulenta. Suppurative inflammations of the tunica vaginalis follow injuries, as well as suppurative processes in the testes and epididymis; in rarer cases they may be hematogenous in origin, as in pyemia.

The most severe extravaginal suppuration which does not involve the testes or the tunica vaginalis is seen in the edematous scrotum of chronic nephritics or in erysipelas or other external infections.

Tuberculous and syphilitic vaginitis were discussed on pages 1490 and 1492 under testis.

Tumors of the spermatic cord and the tunica vaginalis (lit. by Patel and Chalier). In the spermatic cord there have been reported as primary tumors: lipomas (Gabryszewski, Sitzenfrey, Vitrac and Chanaud and others), as large as hens' eggs to men's heads (mistaken for hernias!), fibromas, fibroplasmocytomas (Ciaccio, rare), myxomas, myxofibromas, (Mayer), sarcomas, rhabdomyomas, mixed tumors (see also Naegeli) and very rare dermoids (Wrede, lit., Monti, lit., compare R. Meyer); similar tumors are described in the tunica vaginalis (rare, see also Bayer). In a 30 year old man, the author saw the tunica vaginalis propria of the left testis occupied by a fibrosarcoma in the form of confluent flat nodules (see illustrations in I. Diss. H. Grote). These tumors may be extra- or intravaginal (Kocher). Malignant tumors of the testes invade in continuo or along the veins or lymph vessels (see Most) into the spermatic cord.

Seminal Vesicles and Spermatic Ducts

See Namba, lit. for the histology of these structures and concerning elastic fibers and the pigment in the seminal vesicles.

Inflammations of the seminal vesicles and the vas deferens, vesiculitis or spermatocystitis and deferenitis, are met in the form of mucoid suppurative catarrhs; they are most frequently extensions of inflammations of the urethra, the prostate, bladder, and the epididymis. The gonococcus is the most frequent etiological agent (Lewin and Bohm), particularly in deferenitis (Grosz), but also in spermatocystitis, since the blind-ending depressions and diverticuli of the seminal vesicles offer particularly good hiding places for these organisms. But there also occur hematogenous inflammations of the seminal vesicles, thus in pyemia; a meningococcic spermatocystitis was described by Pick, who also described an acute typhoid prostatitis and spermatocystitis. Vice versa, Gruber and Rossle described pyemia arising from acute staphylomycotic spermatocystitis. The seminal vesicles may be much enlarged from suppuration and contain almost 50 ccm. of pus. If the abscess ruptures into the peritoneal cavity, a suppurative peritonitis follows; the author saw this accident in gonorrhea. Long absence of epithelium leads to atresia of the vas deferens, with ectasia proximal to the obstructed parts. In multiple atresias the spermatic cord may become like a rosary. Obstruction of the spermatic cord naturally produces sterility, but spermatogenesis does not cease, (compare Simmonds, who found increase of the interstitial cells only twice in 40 cases of obstruction of the spermatic ducts).

The infectious granulation tissue tumor of tuberculosis is very frequent in urogenital tuberculosis; it is often bilateral, and according to Teutschlander, more frequent on the right side. But in 84 cases of urogenital tuberculosis, the author found the left seminal vesicle involved 31 times, the right 29 times, and in 24 cases, the condition was bilateral. It has been the primary focus of a tuberculous meningitis; see there. One or both seminal vesicles are enlarged, tough, often surrounded by hard connective tissue; their walls are thickened and caseous or ulcerated; the inner surfaces are irregularly ulcerated, cavernous and soft; caseous-purulent or thickly purulent masses flow out. In other instances, the organs reach the size of hens' eggs, are homogeneous and caseous on section, without any softening, or finally, they may be changed to a sac filled with soft cheesy material. Primary tuberculosis is exceedingly rare; on the other hand, isolated seminal vesicle tuberculosis is not uncommon in tuberculosis elsewhere in the body; (see Gottingen I.—Diss. C. David). The author has seen cases in which, with completely caseous seminal vesicles, a descending tuberculosis of the ejaculatory ducts and the related part of the prostate took place; on the other hand, an infection ascended into the vas deferens, 8 to 9 cm. long, without involving the epididymis and testis; in one of these cases, (14 year old boy with tuberculosis of the lungs), tuberculous meningitis caused his death. Perforation into the pelvic cellular tissue and phlegmon may occur, sometimes with fistulae opening into the anus, the perineum, the rectum, the prostate, or the urinary bladder. The spermatic duct, particularly in the ampulla, is usually involved also; the spermatic cord is changed to a tough, externally fibrous, internally caseous cord, (tubular tuberculosis); it may be widely dilated and soft caseous or creamy masses may be pressed out like worms. In early stages of infection of the spermatic cord coming from the epididymis, subepithelial tubercles are also seen. There also occur cases in which the seminal vesicles have been infected from a tuberculous testis (with the direction of the secretory stream), without changes in the vas deferens. But the seminal vesicles can also be infected from a tuberculous prostate (against the current of secretion); in the infected spermatic cord, the bacilli reach the epididymis by retrograde progression, especially with stasis of secretion from tuberculous narrowing of the spermatic duct. See Simmonds, Zurhelle, and opposed, Sussig, concerning varied forms of seminal vesicle tuberculosis; "bacillary catarrh"—tubercle bacilli from the epididymis reach this structure, increase in number, bring on a catarrh, until later, more severe changes appear in the mucosa. Tuberculosis of the seminal vesicles may also heal; there are then found chalky masses packed in scar tissue adherent to the surroundings.

Cysts appear from the formation of diverticuli. If an ejaculatory duct is obstructed, there occurs hydropic dilatation of the seminal vesicles (hydrops vesiculae seminalis). Emmerich (lit.) saw enormous cysts of the vas deferens.

Calculi (phosphate, carbonate, with organic nuclei) may arise in the seminal vesicles following stasis of secretion. Concretions containing spermatozoa, (spermatic stones), are usually small, white and compressible. Chiari describes rare senile calcification of the ampulla of the vasa deferentia and the seminal vesicles. Eug. Fraenkel saw the same condition in a 45 year old phthisic; the muscle layers become calcified, and, according to Heitzmann, the tunica propria also.

Primary tumors are quite rare; there have been described in the seminal vesicles, carcinoma (see Teubert, lit.; the author has described such a case in an 87 year old man), and sarcoma (Zahn). Ceelen saw a fibromyoma as large as a child's head. The seminal vesicles are more frequently involved by tumors from the neighborhood, thus, from the prostate, rarely from the rectum (Konig); in 23 cases of carcinoma of the prostate, the author saw the seminal vesicles bilaterally involved in 4 cases. See the topographical picture on p. 733. Stoerk and Monckeberg observed rhabdomyomas in the spermatic cord.

Atrophy of the normal seminal vesicles follows defects of the testis and total obstruction of the excretory ducts. If the outflow of secretion is merely hindered, there is dilatation. In seniles, the seminal vesicles undergo atrophy, and become brown, due to an increase of the lipochrome pigments in the epithelial cells which appear at the time of puberty (fat reaction with sudan). The muscle fibers of the walls of the seminal vesicles may contain another kind of brown pigment (Oberndorfer, Namba, lit.).

See Volcker, lit., von Saar, lit. concerning the surgery of the seminal vesicles.

Prostate

Anatomy.—The prostate surrounds the beginning of the urethra (sinus urogenitalis). It is composed of a system of branched tubules ending in blind sacs (Walcker, de Bonis), embedded in a stroma rich in smooth muscle. The glands secrete a clear, glassy, mucoid fluid, the most characteristic component of which is the "prostatic granules" (lit. by Bjorling and s. Fischel and Kreibich). From the beginning of puberty onward as well as in hypertrophy of the prostate, Sehrt constantly found doubly refracting lipoid droplets in the prostatic epithelial cells. According to Kinoshita, however, physiologically the lipoids are mostly of simple composition and decrease about the fiftieth year of life, while larger masses of doubly refracting lipoids first appear in the prostates of older men. In addition to the prostatic glands there are also true mucous glands, which are sparse and perhaps inconstant in adults (Schlachta, lit.). The relative proportion of glands to musculature is so variable (according to Walcker the glands occupy 5/6 of the organ), that even normally, muscular and glandular prostates are differentiated (Waldeyer-Joessel). Through accumulation and thickening of the cross striated muscle fibers toward the urethra, the musculus sphincter vesicae is formed. The prostate is shaped like a chestnut, with its largest diameter oblique, the base toward the bladder, the point resting on the inelastic urogenital diaphragm (fig. B on p. 733); the widest part of the prostate lies behind the urethra, and forms two hazily separated lobules. The middle lobe is a variable structure between the two lateral lobes (lobus medius—pars intermedia—Home's lobe—see lobus pathologicus); it is composed of accessory glands growing under the mucosa of the neck of the bladder. Two larger, and a number of smaller excretory ducts empty on both sides of the colliculus seminalis in the posterior part of the urethra. The prostate also contains the sinus prostaticus (vesicula prostatica, uterus masculinus), a remnant of Muller's ducts in the form of a blind sac which stretches backward into the prostate about 1 to 1½ cm. and empties on the colliculus seminalis (caput gallinaginis) between the ejaculatory ducts. It may occasionally become ectatic and cystic (Englisch, Springer). The lymph vessels of the prostate communicate with those of the urinary bladder and rectum (Bruhns).

According to Lowsley, the development of the prostate begins in the twelfth fetal week from five solid epithelial depressions to the outer side of the pars prostatica urethrae; in later fetal times five lobules are said to be discernible. See Hada (lit.) concerning the development of the prostate.

Inflammations of the Prostate.—The most frequent inflammations are extensions from other urinary and sex organs, thus in gonorrhea of the urethra, in urethral strictures, inflammatory diseases of the bladder, the seminal vesicles, and the rectum. Occasionally a suppurative prostatitis is metastatic in the course of infectious diseases such as typhoid fever, variola and others (see, for example, Wildbolz), pyemia, or even in milder diseases such as angina, parotitis, panaritium; (for example, the author saw it follow furuncles in a 58 year old man), or it is caused by suppurative thrombosis. Acute inflammatory prostatitis may lead to such swelling that dysuria or anuria or even obstruction to defecation occurs. The acute inflammation regresses, becomes chronic and stubborn, particularly in gonorrhea (Moro), or leads to abscesses recognized as fluctuating masses by palpation per rectum.

Prostatorrhoea occurs in chronic prostatitis; it is independent of ejaculation, and consists of the emptying of a thin fluid secretion spontaneously, in drops, or more profusely, during defecation. It may be mistaken for chronic gonorrhea and for spermatorrhea. The sperm is the mixed product of the testes, seminal vesicles, (the secretion of which contains globules like cooked sago), the prostate, and Cowper's glands. The octahedral spermatic crystals (Bottcher, see under lit.), found microscopically in semen which has stood 24 hours, are chiefly products of the prostate; the organic base, spermin, gives to the semen its characteristic odor.

Florence's reaction is useful as an auxiliary method in the examination of spots of semen. On addition of a concentrated solution of iodine (iodine 1.65, potassium iodide 2.54 in 30 cc. of water, accurately!), to semen or the spots of semen, there is quick formation of characteristic brown crystals (Gumprecht). See Cevidalli concerning Barberio's microchemical reaction of semen.

Abscesses in the prostate may be acute or insidious. Small abscesses heal spontaneously, usually after perforation into the urethra. Occasionally several small abscesses coalesce, so that a many-cornered abscess cavity arises which then empties into the urethra through multiple perforations. Periprostatitis phlegmonosa is a frequent consequence. The rupture of the abscesses may then occur into the rectum, toward the perineum, or, more rarely, into the peritoneal cavity (lit. by Lipowski).

See Cholzow for gonococcus septicemia from gonorrheal prostatic abscesses; Socin believes the gonococci enter the blood via small veins.

Tuberculosis of the Prostate.—Tuberculosis frequently begins in the depths of the prostate, but the canals of the genital system which open into the pars prostatica of the urethra are often previously involved. It occurs in the form of miliary nodules or larger caseous masses scattered everywhere throughout the organ; when their centers soften, caseous cavities develop with fibrosed outer layers. Perforation into neighboring cavities is frequent, particularly into the prostatic part of the urethra. And the urethra is occasionally involved throughout its entire length. Rupture into the rectum is rarer, but may occur through multiple fistulae. The prostate is usually but little enlarged. Larger organs, hen's egg size or more, occur in the cases with stiff caseation without softening, in which the seminal vesicles and testes are usually also involved (p. 1488).

Tuberculosis of the prostate is more common than is macroscopically evident (compare Tietze). It is very frequent in urogenital tuberculosis; in 59 cases, the author saw it in 49 (83%); more rarely it is isolated, without tuberculous testes or epididymis (Koch, Gotzl and others). According to Simmonds, primary genital tuberculosis starts in the prostate in 50% of the cases, in 25% from the seminal vesicles and epididymis, and from these centers it spreads in testifugal and testipetal directions. The central position of the prostate in the urogenital system makes it clear that it may be infected from both the urinary and genital organs, and that it may become a distributing station from the sex organs to the kidneys, or vice versa. On the other hand, it is also possible that hematogenous involvement, usually from the lungs, (compare Simmonds), or from the urethra, can initiate an ascending infection toward the kidneys, or a descending infection toward the testes. But the author has seen cases in which only a part of one vas deferens, the ejaculatory duct, or only one seminal vesicle, was infected from a much involved prostate, while the epididymis and testes, and the bladder, ureters and kidneys, were completely intact (compare I.—Diss. Rautberd, Basel 1908). Such cases demonstrate the possibility of a testipetal ascending genital tuberculosis (Gotzl, Benda, Pratorius, Walker), in which the factors are both the intimate relationship of the lymph vessels and the antiperistaltic movements in the vas deferens, such as have been demonstrated in animals; stasis of secretion favors ascending infection. Even v. Baumgarten, who, on the basis of experimental and anatomic observations, expressed the opinion that tuberculosis of the urogenital apparatus never extends against the secretory current, but always in the direction of these streams (see also Kraemer), recognizes exceptions when stasis is present. Sangiorgi believes in the possibility of an intracanalicular ascent from the prostate and vas deferens to the epididymis, when, *e.g.*, the normal flow of secretion is disturbed from the mechanical hindrances of severe diseases of the testis. Cholzoff, on the other hand, is of the opinion that the place of primary localization, from which the remaining sex organs are infected, is in the prostate as well as the epididymis, seminal vesicles, and that in the bilateral form the spread from the one to the other side may take place through the blood and lymph vessels as well as through the vas deferens. Concerning the mode of spread of urogenital tuberculosis, compare pages 1515, 1489, 1431, 1367 under testes, bladder, seminal vesicles, kidneys; see there for literature. See also extensive literature concerning tuberculosis of the prostate by Hesse.

Foreign body giant cells may collect around the corpora amylacea, and be mistaken for tubercles, since they occur also in the tuberculous prostate (Wieke, Orth).

Little is known concerning syphilis of the prostate and that mostly from the clinical point of view. Cohn has described an inflammatory destructive change (see also Handbuch d. Urologie from von Frisch, Vol. 3).

See Th. Cohn concerning actinomycosis of the prostate, bladder and the pelvis.

Concrements of the Prostate and Regressive Changes. Concrements.—Cross sections of the prostates of older men contain almost constant yellow or brown to black granules like snuff or poppy seeds lying more or less loosely in small spaces. Rarely, stones the size of peas or larger may be felt through the rectum.

Most of the stones reported in the literature as weighing 300 to 400 grams are in reality urinary stones which became embedded in the prostate; compare Socin-E. Burchkhardt (lit.). The stone weighing 320 grams reported by Ravasini probably also belongs in this class.

Microscopically, the lumena contain small rounded or angular nodules, some of which stain blue with iodine as amyloid bodies, and some of which stain merely yellow, brown or green; they are composed of concentrically, occasionally radiating, stripes (corpora amylacea), as well as of hyalin spheres and cylinders (fig. 784) from the confluence of hyalin droplets. The larger granules are darker and occasionally contain calcium salts in addition to an albuminous nucleus. These concrements are composed of the hyalinized protoplasm of dead and desquamated epithelial cells (Stilling); Weski believes they are "secretion tears" (hyalin intracellular bodies which Stilling also has seen). The smallest nodules occur even in children, but are rare, and composed only of pale hyalin flakes (Stilling, Lachowsky). Later they become more and more yellow to brown. Their staining reactions are quite varied; according to Bering, it depends upon the content of organic material. They may also become the nuclei of larger true calcium-containing stones (prostatic calculi), which are as large as poppy seeds, rounded or cactus-like; they remain in the excretory ducts and are occasionally present in large numbers. Rarely, larger stones reach the urethra and are obstructed in their passage. The epithelial cells of the prostate contain increasing amounts of yellow pigment granules with increasing age (lipoid or excretory pigment, Ishihara). The dark pigment of the nodules comes from this source.

Regressive Changes.—Fatty degeneration of the epithelial and muscle cells with hyalinization, concrement formation, brown pigmentation, probably lipoid, as well as hyalin changes of the muscle fibers in the connective tissue walls of the canals, take place as age increases and as a presenile condition after febrile diseases, etc.

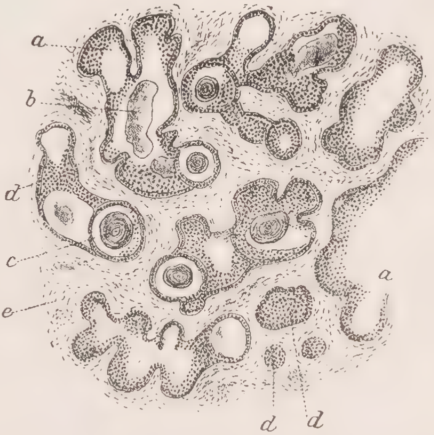


Fig. 784.—From a glandular-hypertrophic prostate with concretions; a, glands; b, hyalin cylindrical coagula in lumen; c, laminated concretions; d, gland surface section; e, fibromuscular stroma. (Med. magn.)

Atrophy of the entire prostate occurs in marasmus, atrophy of the testes, in orchitis, and after castration. The latter statement has been repeatedly confirmed in animals, and this theory has been used in the treatment of hypertrophy of the prostate (castration or resection of the vas deferens); such operative procedures are said to bring about diminution in size of the prostate through fatty degeneration of all the tissues (Griffith); v. Frisch, however, doubts the truth of this statement; the method has been abandoned. In malformations, (misplacement of the testes), the prostate frequently remains infantile. Generally, it reaches its largest development when puberty is fully established.

So-called Hypertrophy and Tumors of the Prostate.—By so-called hypertrophy of the prostate is understood a rather common, slowly increasing enlargement, occurring particularly in advanced age, but occasionally at the fortieth year of life. Enlargement, however, is not uniform in all parts, even though the organ reaches the size of a fist; the section surface always shows embedded nodules in which the encapsulated remnants of glands can still be differentiated (fig. 786); in other cases single parts are enlarged and nodular, particularly the so-called middle lobe which is prominent as a cherry, egg or walnut sized tumor at the base of the bladder (figs. 785 and 787).

Not all old men become prostatics with urinary bladder difficulties; on the contrary, according to the views of most clinicians (Paul, v. Dittel), the prostate becomes smaller in the great majority of old men; even if this does not occur, (the anatomical statistics, to the contrary, show that hypertrophy takes place in 50% of all old men), the enlargement may give no trouble. After deletion of the cases with pathological increase in size, Simmonds found that the normal weight from the sixth to the eighth decades fell from 18 grams to 15 grams, and he confirmed the old opinion of the physiological atrophy of age to which many cases of incontinence in marantic seniles is due (Dittel, cited by Hochenegg); but, as before, most cases give no trouble. Thompson believes a prostate weighing over 27 grams is pathological; the weight may reach 100 grams.

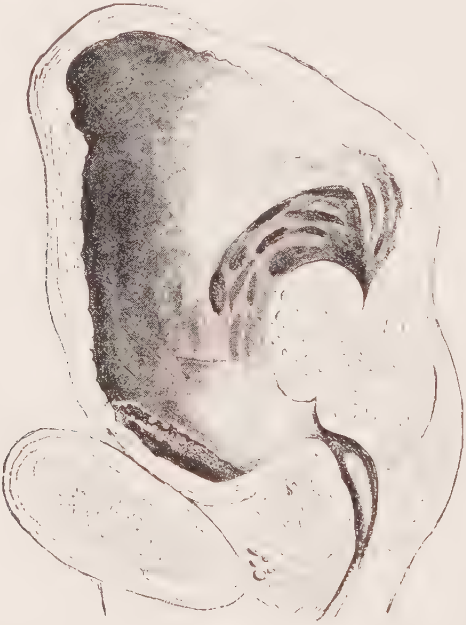


FIG. 785.—Hypertrophy of the so-called Hume's lobe (middle lobe) of prostate. Obvious glands and cysts in the lobe which projects into the bladder; bladder dilated and hypertrophic, with numerous niches; prostatic urethra of normal width and curvature; symphysis in front; man of 74 years with cystitis and pyelonephritis. Specimen hardened in chromic acid, median section; ⅔ nat. size.

Ciechanowski, partly confirming the belief of others, and partly opposing them (see lit. in appendix), believes the chief cause of intumescence is a chronic, inflammation of the prostate, usually gonorrheal (p. 1525). But Keyes doubts the causative relationship of gonorrhea, because hypertrophy of the prostate is such a rare condition in comparison to the frequency of gonorrhea, and because it occurs so much later; in 433 cases of hypertrophy, there were only 18 in whom clinical symptoms were manifested. Raskai and Lanz, Lissauer, also doubt the conception of Ciechanowski. Others speak, with Virchow, of tumor, others of involution hypertrophy (p. 1527). According to Furbringer, the cause of prostatic hypertrophy is not as yet known.

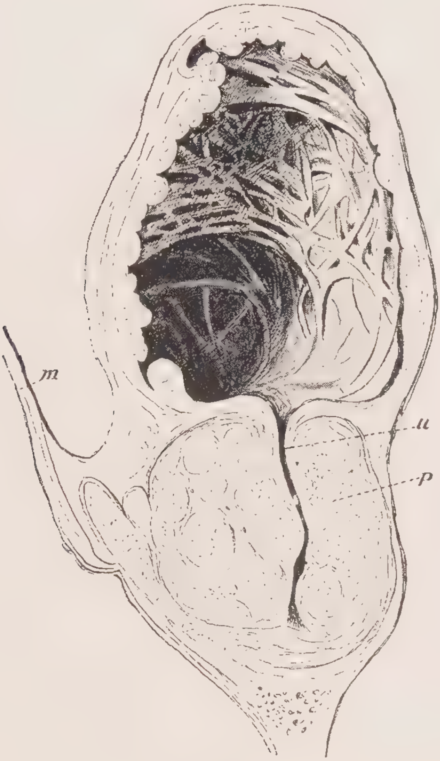


FIG. 786.—Trabecular hypertrophy of bladder with marked, mostly glandular, hypertrophy of prostate (p); u, curved course of prostatic urethra; m, anterior wall of rectum; man of 83 years with pyelonephritis; median sect. of spec. hardened in chromic acid, l. half; ⅔ nat. size.

Diffuse hypertrophy, chiefly from dilatation of the glands as consequences of an inflammatory interstitial connective tissue overgrowth, is an exception; typical so-called hypertrophy is accompanied by circumscribed nodule formation.

The nodules may be enucleated, and therein they are similar to fibroadenomas of the breast, myomas in the uterus and the nodules in the thyroid; there then remains an uneven fibrous bed in the actual prostatic tissue.

The composition of a nodule is usually glandulo-fibromuscular, the epithelial glandular parts predominating and the fibrous and muscular parts present in varying quantities. Predominantly, or pure fibromuscular nodules are much more rare. The purely glandular medullary forms are also fairly uncommon.

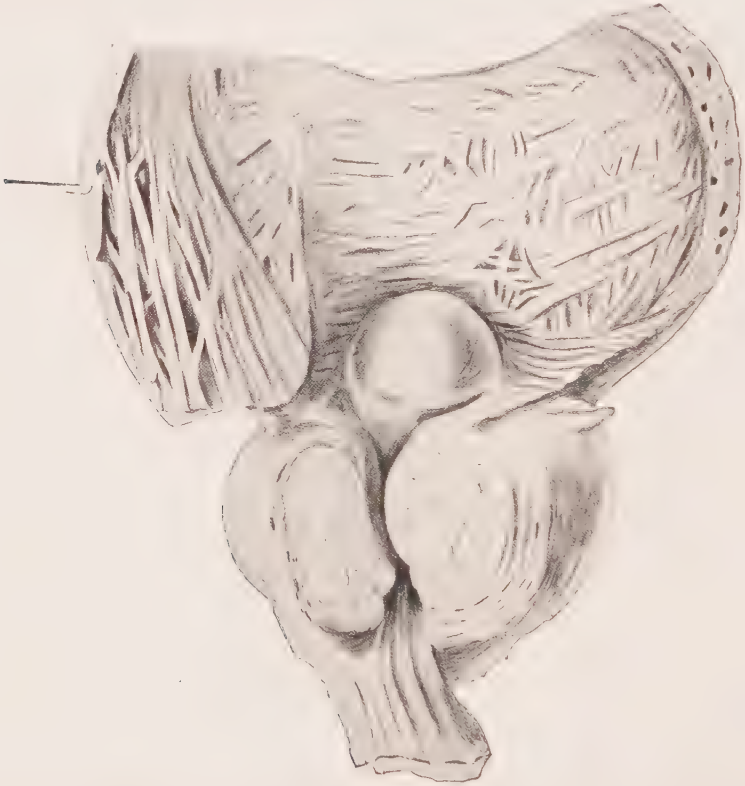


Fig. 787.—Marked hypertrophy of prostate with valve-like or cork-like middle lobe, so-called trabeculated bladder. The displaced lateral lobe forms a capsule around the nodules; cystitis and pyelonephritis; man 83 years old; $\frac{2}{3}$ nat. size.

What are the points of origin, or the anatomical situations of the so-called hypertrophy?

Opinions concerning this question are still much divided. Jores emphasizes that "hypertrophy of the middle lobe" is in reality not a disease of the middle lobe merely because it is first seen when pathological, *i.e.*, when its enlargement makes it appear as an actual lobe, but the condition is a pushing forward of accessory glands found normally under the mucosa of the bladder and in the prostatic parts of the urethra. According to the views of Tandler and Zuckerkandl, with which the views of

Simmonds agree, the typical enucleated nodules do not come from the prostate itself, but from accessory glands which normally surround the urethra between the sphincter of the bladder and caput gallinaginis. Previously, Motz and Pereanau, among others, had also assumed that hypertrophy took place at the cost of the central periurethral glands. According to Ribbert, however, the chief point of interest lies in glands belonging to the lateral lobes arranged around the colliculus alongside of the urethra; all other parts of the prostate, as well as the accessory glands in the upper part of the urethra are of little importance in the origin of these nodules (adenomas). Loeschke differentiates (*a*) submucous periurethral, (*b*) internal glands further away from the urethra, (*c*) external glands; he emphasizes the role of the internal glands, and Neimeyer and Adrion (lit.) follow his lead. According to Adrion, the internal glands are composed of lobules embedded in the muscle layers and spreading with the bladder musculature into the pars prostatica urethrae, and thus into the prostate itself; they are thus predisposed to nodular boundaries in cases of enlargement; thick muscle bundles surround the sharply outlined, easily enucleated, adenomatous nodules. After breaking through the muscle layers they may grow in the direction of the base of the bladder and thus produce the valve-like middle lobe, or toward the urethra and simulate enlargement of the periurethral glands; their enlargement causes the latter to tear the urethra and compromise the tissues of the prostate which then cover the nodules like a capsule (fig. 787). The external glands do not build nodules, but if they become hyperplastic, produce a spongy network. The periurethral glands therefore play no part in the condition, (Lendorf, Grinenko), contrary to the opinion of many that they alone are the points of origin of so-called hypertrophy of the prostate.

According to Ciechanowski, however, the so-called hypertrophy occurs only in this wise: following inflammatory productive connective tissue overgrowth in the neighborhood of the excretory ducts, there is retention of secretion and dilatation of the peripheral gland branches. Gonorrhea is a frequent cause. Fresh infiltrative foci are very frequent in the interstitial tissue as Greene and Brooks have confirmed. At the same time, there also occur endo-glandular pathological processes consisting of vigorous proliferation and desquamation of epithelium. Leucocytes, colloid masses and concrements are found in the gland lumena. Ciechanowski believes these processes are a catarrhal inflammation, and that the hypertrophy is due almost exclusively to dilatation of the glands. But Greene and Brooks in a large number of cases found a fibrous hyperplasia destroying the musculature and the glands as an expression of chronic inflammation, and the cause of enlargement; in only a minority of the cases did they find cystic dilatation of the glands as the chief change.

Although the periglandular infiltrates, etc., as described by Ciechanowski, have been confirmed by Rothschild and others, Finger found them but seldom, and Wichmann determined that the ectasy of glands is the chief cause of the enlargement in only isolated cases, and then seldom directly from infiltrates. On the other hand, Halle and Albarran call attention to the dominant part played by the glandular growth, and speak of tumor-like adenomatous hypertrophy, which frequently leads to carcinoma, too frequently, of course, from our viewpoint. Cosentino recognizes only a mixed form. It is quite obvious, as stated above, that there are a number of forms of so-called hypertrophy; a glandular, which macroscopically and microscopically, is a glandular cystic process of many forms; a fibro-muscular to fibrous form in which the glandular structures are secondary; and finally a fibroglandular or a fibro-musculo-glandular form. It also seems possible that the glandular form may eventually become the smooth, tougher form. Exceptionally, the enlargement may be due chiefly to dilatation of the glands which increases in old age.

In the most frequent form, *i.e.*, the so-called glandular hypertrophy, the fibro-muscular parts are also involved, and there are multiple islands of actual prostatic tissue surrounded by concentric layers of interstitial tissue or by capsule-like connective tissue. The ducts are dilated and the glands are in isolated complexes, which on section appear gray-yellow, soft, nodular, perhaps cystic, and prominent on the surface. Microscopically, the gland tubules are irregular and branched, many are dilated and cystic, and many are filled with concrements (figs. 784 and 785); the connective tissue shows a varying proportion of fibrous and fibro-muscular parts. The rarer, so-called fibro-muscular hypertrophies are sometimes more fibrous and sometimes more muscular. The former are harder and may be cicatricial. Gray-white section surfaces are ofttimes nodular, in other cases more homogeneous; microscopically, the glands are isolated. Chronic inflammatory changes in the glands and interstitial tissue are very frequent and may be accidental, but are believed by many to be of etiological importance in the hypertrophy; most authors disagree with this view (see also Young, Geraghty and others). Venous stasis is practically always present.

Whatever the cause, it is certain that it is not a simple hypertrophy. Many speak of a compensatory or a regenerative tumor-like hyperplasia (Hada); others, *e.g.*, Veszpremi, of an intumescentia senilis (nodosa or diffusa). Tsunoda believes it is a true neoplasm, a view which Virchow championed, and he speaks of a kind of strumous structure; Rungel Knyjer, Ribbert, Legueu, the latter of whom claims he found a local eosinophilia which is absent in prostatic carcinomas, speak directly of adenoma. Paul emphasizes the involution idea analogous to "involution hypertrophy" of the breast. In both organs there occur the same climacteric influences bringing about small cell inflammatory infiltrates as well as chronic changes in the glands, such as hypertrophy of the epithelium, cysts, and intracystic growths. Both the prostate and the breast are said to exhibit the same tendency to excessive cancerous growth of the acini. The author believes this viewpoint is worthy of notice; the involution, perhaps, is the first stimulus to nodule formation.

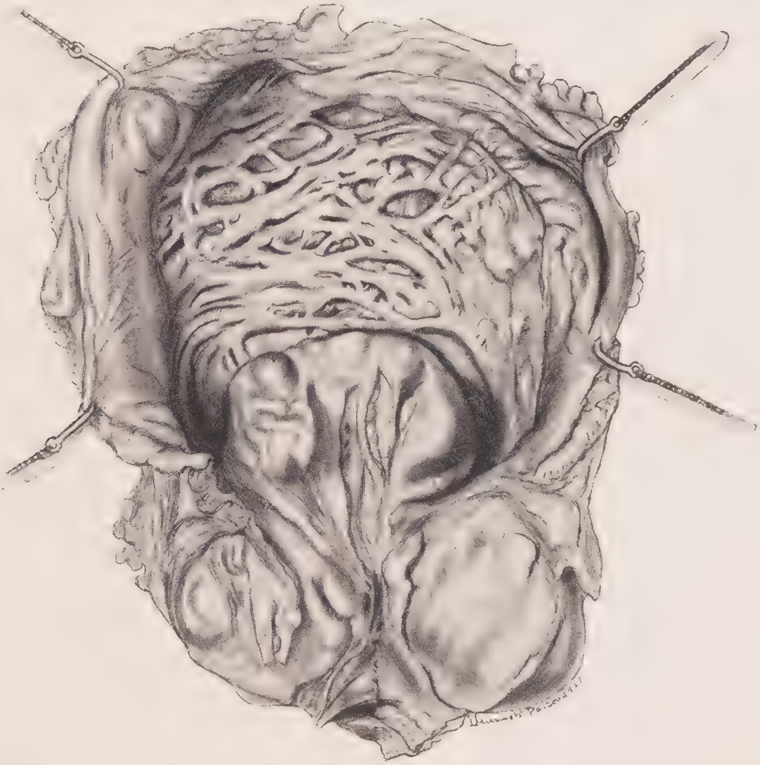


FIG. 788.—Enlarged prostate in man 86 years old. This patient had suffered from urinary difficulties for six years controlled by occasional catheterization and local treatment of the bladder. On account of general reasons he was not operated. He died of uremia consequent to kidney destruction from bilateral progressive hydronephrosis. The enlarged median lobe of the prostate as seen in the drawing compressed the openings of the ureters and made difficult the outflow of urine from the kidneys. There is the usual trabeculation of the bladder wall. Probably the muscularis was thicker at one time than it was when the specimen was removed when considerable atrophy of the muscularis had taken place. The amount of infection present in the urinary tract was a minimum. This illustrates one of the complications of enlarged prostate. The relative absence of infection, especially when catheterization was frequent, is unusual. L. H. #262. ½ nat. size.

Simmonds is inclined to believe that it is a compensatory affair inasmuch as accessory periurethral glands may take over the functional activities of the atrophic gland in the aged. Niemeyer, however, considers this applicable only in cases of mild hypertrophy; in advanced hypertrophy, he thinks, like most authors, that there is tumor formation.

That a carcinoma either of the adeno- or the solid type may arise from the vigorously growing epithelium in these glandular nodules cannot, of course, be denied.

As is well known, recurrences sometimes occur after prostatectomy for hypertrophy (compare lit. by Socin-E. Burckhardt, Lumpert); this is believed to be a particularly good proof of the neoplastic nature of the changes (Chiari). But another interpretation may be placed upon this, viz., that complexes which at first were resting, later become nodular.

The remarkable rejuvenation of the organism which occasionally follows removal of prostatic nodules is, as Blum states, not a Steinach effect (p. 1482), because the spermatic and the ejaculatory ducts are not obstructed; the proper operation tears these parts; it is probably a consequence of the removal of pressure of the nodules on those structures, as well as a regeneration of the tissues previously compromised by the nodules; thus new hormones may be released to the body.

The chief consequences of hypertrophy are narrowing and angular kinking of the prostatic part of the urethra with mechanical hindrance to the outflow of urine. If the middle lobe is nodular, it may act as a valve or a lid on the sinus urogenitalis, which is more tightly closed as the bladder is filled (barriere prostatique, Mercier). Similarly, a bladder valve may form a barrier, as Eigenbrodt and Trendelenburg describe in their cases; a fold of the mucous membrane approximately 1 cm. high (according to Brommer, lit., it is muscular), situated behind the internal orifice, acts as the valve, so that finally it is utterly impossible to void when the bladder is filled; the catheter meets with no obstruction but there is much residual urine and much urgency. Cause: probably congenital hyperplasias. Congenital valve-like mucous membrane folds occur at the colliculus seminalis and may obstruct the urine. (Compare lit. by E. Burckhardt, Lindemann, Lederer.) See under ureteral cysts, p. 1297.

As a further result of hypertrophy, the musculature of the badder wall hypertrophies, remains vigorous for a long time, thus becoming trabeculated, finally with diverticuli and pockets (p. 1444), but eventually the organ is overstretched, becomes more and more atonic, reaches an enormous degree of dilatation, the walls become thin and relaxed and the trabeculae almost entirely smoothed out. Hematuria is quite frequent, provoked either by catheterization or by rupture of varicose veins in the mucosa. Cystitis frequently follows catheterization. Another serious result is urinary stasis (p. 1403), with polyuria and its consequences, hydronephrosis, and pyelonephritis.

Tandler and Zuckerkandl call attention to the narrow part of the ureter where it crosses the vas deferens.

Polyuria is probably reflex from the urinary passages, *i.e.*, from a filled bladder, catheter, frequent micturition; the urine has a low specific gravity, is poor in chlorine and nitrogen, may reach the amount of 8 to 10 liters per day, and the condition be mistaken for diabetes insipidus. The final results are dehydration of the tissues, thickening of the blood, constipation, emaciation, cachexia; these changes explain the fact that sudden deaths occur spontaneously or after operative procedures (Lichtwitz, Duttmann).

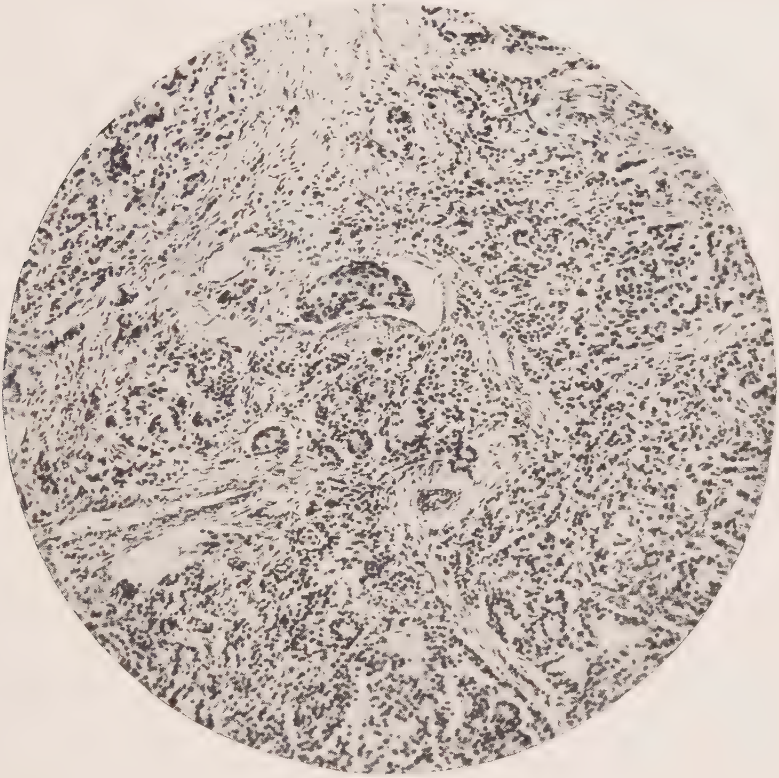


FIG. 789.—Carcinoma of the prostate showing tumor thrombosis in vessels. Carcinomas of the prostate are notorious for producing metastases in the skeleton. "Accidents" like this bring to grief many of our efforts at tumor "grading." L. H. #480.

False passages through the urethra, (p. 1455), produced by catheters, are particularly frequent in hypertrophy of the so-called middle lobe which may have a number of tunnels bored through it.

Malignant Tumors of the Prostate (Lit. in Appendix).—Carcinoma of the prostate is very important and in no wise rare. The macroscopic differentiation from glandular hypertrophy is often difficult, particularly when the carcinoma has small tendency to invade the neighborhood and to softening; usually the organ becomes hard and dense, though unchanged in form and size for some time; sometimes it gives the impression of a colossal hypertrophy. The yellow color of the primary prostatic tumor and the metastases depends upon the presence of doubly refracting lipoids (Schlagenhaufer; p. 1517); Kinoshita speaks of carcinoma xanthomatodes. Softening, when present, is a complicated suppuration or liquefaction. Many of these tumors are so small that they are overlooked; cachexia, and metastases in the skeletal system may be the first manifestations.

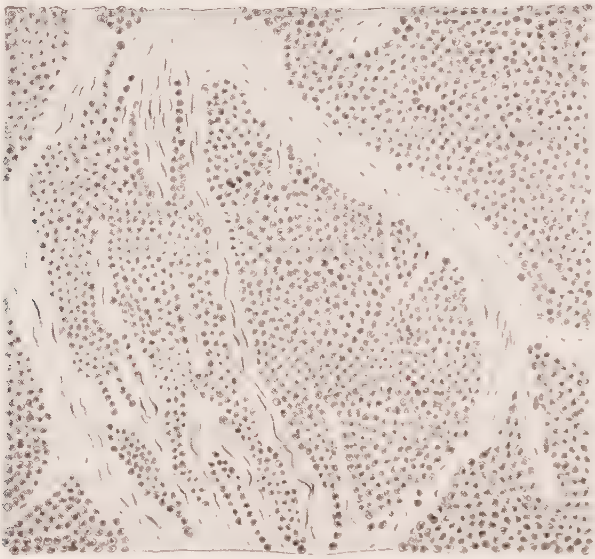


Fig. 790.—Solid carcinoma of prostate, growing in larger and smaller cell nests and even in single cell rows throughout the fibromuscular tissue of the organ. To the right above, in the center of a solid cell complex is a gland-like lumen; man of 77 years with osteoplastic skeletal carcinosis.

When extension takes place through the lymph channels the bladder is quickly involved, but, as a rule, the posterior wall is merely diffusely infiltrated with small nodular or hemispherical prominences jutting into the lumen; perforation is quite rare (avoid mistaking for primary bladder carcinoma). The seminal vesicles are invaded; the carcinoma seldom reaches the urethra—but the author has seen retrograde submucous transport through the lymph channels—or the rectum, which is remarkable, inasmuch as the lymph channels of the prostate communicate with those of the rectum, bladder and vas deferens (Bruhns). By compression the tumor compromises neighboring organs. The forms which spread rapidly through the soft parts of the neighborhood and into the bony pelvis are less frequent; they have been called by Guyon "carcinose prostato-pelvienne;" they cannot be taken intra vitam for anything other than malignant tumors. The carcinomatous organs are as though cemented into the pelvis.

Metastases are frequent to the regional and even distant lymph nodes; v. Baumgarten and Lundsgaard described generalized lymph node metastases clinically mistaken for lymphomata maligna or lymphomatosis; there is less tendency to metastasis in internal organs. But the latter has been seen frequently enough by the author. The preference for early metastasis to the skeleton is quite remarkable, and occurs particularly in the form of an ossifying carcinosis (v. Recklinghausen), see figs. 639, 640, 641, pages 1222 and 1224. (This is quite frequent also in carcinoma of the breast, but usually the metastases appear later.) Among 24 cases of prostatic carcinoma (the author, and W. Courvoisier 22 cases), there were bone metastases in 10, and the ossifying character was noted in 8.

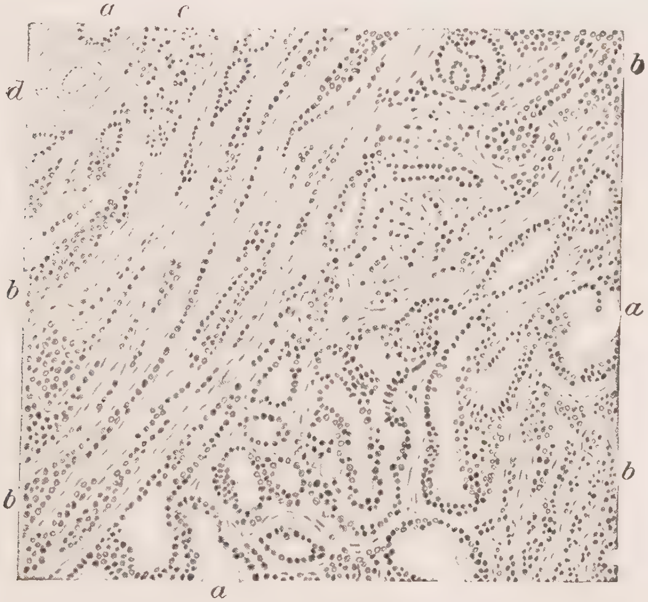


FIG. 791.—Adenocarcinoma of prostate with transition into carcinoma solidum; a, gland imitations; b, solid cell plugs and cell columns; c, smooth muscle bundles around nests; d, vein; man 75 years of age.

The same microscopic section may show typical adenocarcinoma alongside of simple solid or scirrhous growth; or large masses of irregular cells constitute a medullary tumor. The cells of the solid variety are usually small, polygonal or rounded (fig. 790), and show a particular tendency to infiltrate into the tissue spaces. But an infiltrating growth does occur in the adeno forms. Both forms are frequently combined and this irregularity can be put to use in the differential diagnosis between carcinoma and glandular hypertrophy. The tubes of the adeno-carcinoma contain epithelial detritus; concrements are usually, but not always, absent. The interstitial tissue containing focal masses of smooth muscle, fig. 791), is, in general, rich in spindle and round cells. Squamous cell carcinomas have also been described (Buchal), and are particularly interesting in relation to the statements of Aschoff and Schlachta, that the prostate of the fetus and newborn contains much layered squamous epithelium, which occasionally persists and is accompanied by the formation of crenated cells, keratohyalin and cornification (Schmidt, lit.). Lubarsch, Schridde, describe squamous epithelium in adenocarcinomas, a finding confirmed by the author. Prostatic carcinomas are seldom found before the fortieth year, although Gardner and Cummins described an example in a 17 year old boy, Lang and Krainz in a 26 year old, Willan in a 28 year old, Weinert in a 38 year old man; the highest frequency is in the seventh decade. The older view that carcinoma of the prostate is frequent in children is erroneous; there has been no certain case of this kind reported. The views of Steffen do not withstand criticism.

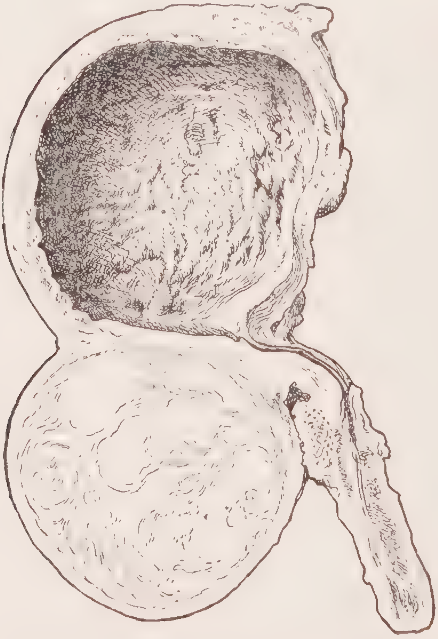


FIG. 792.—Rhabdomyoma of prostate from a 9 mo. old child; hypertrophy of bladder. (Deutsche Chir. No. 53. 1902); nat. size.

Sarcomas of the prostate, observed even in children (lit. by W. H. Schultze), are much less frequent; their size is relatively more important than that of carcinomas and may reach, in exceptional cases, that of a child's head (Socin). They endanger the neighboring organs by pressure and invasion, and often show a tendency to spread toward the perineum. Infiltration of lymph nodes and distant metastases are usually absent, although we have seen cases with extensive secondary growths. (See Socin and E. Burckhardt, Deutsch. Chir., Lief. 53, 1902.) The course is rapid, as in an observation of the author, a round cell sarcoma of the trabeculated bladder of a 4¾ year old boy, died with urinary difficulties in 8 weeks, (Journ. No. 660, 1415). Histologically they are quite varied. Round and spindle cell types are the most frequent. But among 8 cases, the author saw an angiosarcoma (Pleschner, lit.), lymphosarcoma, myxosarcoma and, as hitherto undescribed tumor forms, 3 malignant rhabdomyomas (fig. 792). Mixed tumors are very rare. Giani described a mixed tumor with cross striated and smooth muscle fibers and glands; Birch-Hirschfeld described an adenosarcoma, Kapsammer a small cell sarcoma with islands of cartilage, Mogi an osteoplastic angiosarcoma, Kinoshita a carcinoma sarcomatodes with islands of cartilage.

Secondary tumors of the prostate are rare. They usually appear by direct extension from carcinomas of the rectum or the bladder, and exceptionally from the seminal vesicles. An interesting secondary sarcoma arising in the rectum is described on p. 826. Undoubted cases of metastases coming from distant organs are present in the literature, including a short note in Henke's Geschwulstdiagnostic concerning a case in melanosarcomatosis. In a 48 year old man with melanosarcomatosis (mentioned pages 879 and 1008), the author saw a black sarcoma nodule as large as a lentil in the central part of the right lobe.

Animal parasites are very rare. Echinococci have been observed. Lit. by Hesse.

Penis and Scrotum

For **malformations,** see p. 1477. For the innervation of the male sex organs, see L. R. Muller and Dahl.

Inflammations involve the external skin or the inner layer of the prepuce (posthitis), the surface of the glans, (balanitis), or the corpora cavernosa (cavernitis).

When the scrotum becomes edematous, particularly in kidney disease, it is swollen, stiffened, and thickened and, because of decreased resistance, is a frequent victim of phlegmons and gangrene.

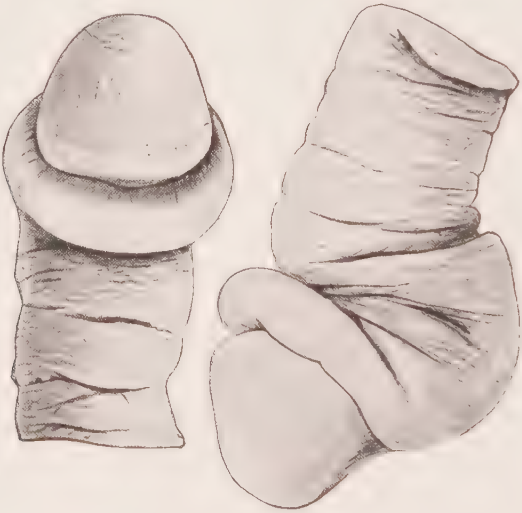
Gangrene of the penis and scrotum occurs as the so-called spontaneous type during the course of general infections such as typhoid fever, variola, etc., as well as without previous edema in the presence of local inflammatory processes. W. H. Schultze described a case occurring during erysipelas in which there was partial necrosis of the penis and scrotum with exposure of one testis. For more details, see Kuttner; and see genital gangrene by Coenen and Przedborski (lit.).

Induratio penis plastica is described on p. 1535.

Balanitis and posthitis are often a result of uncleanliness and decomposition of the smegma which accumulates under the prepuce in the retroglandular sulcus.

This sebaceous-like white material is composed almost exclusively of desquamated epidermis cells mixed in small numbers with the secretion of the small, poorly developed, preputial sebaceous glands (Tyson's glands). The latter are situated on the glans penis and in the lamina interna praeputii (Saalfeld), and, according to Eberth, in a small transitional zone of the outer leaf of the prepuce into the inner layer (Boyd, Grosz). See p. 1452 concerning their relation to gonorrhea.

Considerable practical importance is credited to the bacteria in the smegma of healthy individuals, male as well as female; these so-called non-pathogenic smegma bacilli, (Matterstock, Alvares and Tavel), are similar, perhaps identical, with the erroneously called syphilis bacillus (Lustgarten); but more important, they are similar to the tubercle bacillus in their staining reactions (for staining, see p. 422; consult urine in tuberculosis of the kidneys, p. 1372). In the differentiation from true tubercle bacilli, the smegma bacilli are more easily decolorized by acid alcohol. See Lipp, concerning the staining of tubercle bacilli by corallin. But definite separation is possible only through culture and animal inoculation (A. Weber, Salus; Schuster).



FIGS. 793 and 794.—Paraphimosis in a man 87 years old (with spondylitis tuberculosa) anterior and lateral view; ¾ nat. size.

Since these parts are always bathed in pus in urethral gonorrhea and ulcerative chancres, there is always a secondary balanoposthitis, particularly in individuals who have long narrow snout-like prepuces. (Consult congenital phimosis, p. 1577.) With redness and swelling of the part, there accumulates an exudate on the surface. The epithelium is desquamated (erosion). If the swelling reaches considerable degree, it may produce an inflammatory phimosis; if the swelling reaches excessive degree, the inflammatory phimosis prevents exposure of the glans. Deeper ulcerations and necroses may progress from the erosions. When healing occurs, the glans adheres to the prepuce.

See p. 1538 for leukoplacia penis.

By paraphimosis is understood a condition in which the prepuce, when pushed back, can no longer be replaced; this usually is a result of phimosis; because of its short inner leaf, the prepuce becomes tight in the sulcus behind the glans. The latter grows cyanotic, edematous, swollen; the edematous foreskin itself surrounds the corona like a thick ring or collar. If the condition is not treated surgically by incision, gangrene or necrosis soon ensues of the glans and the prepuce. The posterior part of the prepuce may ulcerate and the glans protrude through the opening.

Changes in the Corpora Cavernosa.—Cavernitis, or deep inflammation of the penis, may follow traumata, inflammations spread from the urethra, such as gonorrhea, or, more rarely, infectious diseases such as typhoid fever, pyemia, etc. There are suppuration, abscess formation, and gangrene, with urine infiltration and the formation of fistulae. Priapism may also occur. Healing is followed by deforming scars, perhaps interfering with erection. Partial ossification of cicatrized parts takes place at times. Injuries of the corpora cavernosa from tears by kinking (fracture of penis), crushes, external wounds, are usually accompanied by hemorrhage; there is danger of urine infiltration and the development of deforming scars after healing. Scars destroy a number of blood spaces, which then take no part in erection and the penis becomes crooked. Autochthonous thrombosis, *i.e.*, the formation of white thrombi poor in fibrin in the corpora cavernosa, interferes with the emptying of these structures and is followed by connective tissue induration; leukemic priapism (Kauders, Kast, Stanjek) occasionally lasts for weeks; it is occasionally observed in hemophilia, pyemia, typhoid fever, gout, traumatic hemorrhage with thrombosis, neoplasms, etc.; (see Goebel, Blum, Terrier and Dujarier, lit. F. Rosenthal; for lit. concerning priapism, see Scheuer). Metastatic sarcomas and carcinomas are quite rare; but secondary tumors by invasion, particularly from the prostate, are not uncommon; also from the rectum.

Induratio penis plastica consists of spotted hyperplasias of the connective tissue, which, according to Wiedkopf, originate from the adventitia of the capillaries. In older stages, there are nodules of cartilage and bone. (See Gerster and Mandlebaum concerning bone formation in the penis.) The condition may also involve the corpora cavernosa after beginning on the back of the penis in the form of cartilaginous connective tissue plates under the unchanged skin; it usually occurs in old age; changes in the elastic tissue in the spaces of the penis are important preliminaries (Werth and Scheele). See also Delblanco, Sonntag, lit.

Soft Chancres, Ulcus Molle.—Soft chancres (see under skin) are highly infectious, but not syphilitic, and are caused by the transfer of material from the ulcers during coitus; they occur usually on the foreskin, on the frenulum, and on the glans. Suppurative bubo is a common consequence (p. 252).

The characteristics are: a rounded defect with sharply outlined, indented, always soft, edges, which may be undermined; the base is uneven and covered with necrotic tissue and pus. The causative organisms are the highly contagious Ducrey's streptobacilli. The infection spreads rapidly into the neighborhood (scrotum, thighs, abdominal skin), as multiple chancroids. The scars of healing are flat and quite shallow. The most severe form, the phagedenic ulcer, produces marked tissue destruction, and the deep scars from this condition produce marked deformities.

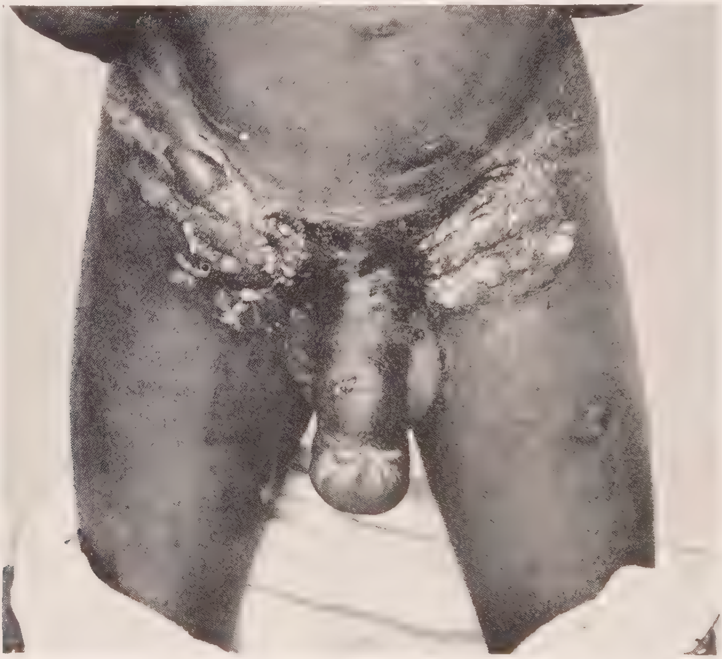


FIG. 795.—Granuloma inguinale. Courtesy of Dr. W. F. Mackinney. L. H.

Occasionally there is a particularly narrow phimosis in soft chancre (Rille).

Infectious Granulation Tumors (Syphilis and Tuberculosis). Syphilitic Initial Lesions.—In the male the penis is the most frequent site of the primary lesion; the corona and frenulum are the favorite points. The inner leaf of the prepuce becomes scaly, and as the flat infiltrate undergoes destruction, there appears the hard chancre. Healing usually leaves no residue; occasionally, however, there are rounded or angular depressions in the surface of the glans.

Secondary syphilides as papules, which are called condylomata lata, when they reach a certain extent, occur on the mucous membrane and the external skin of the glans and the scrotum. They are much less common in the male genitalia.

Gummata in tertiary syphilis occur in the glans and the corpora cavernosa, resulting in very extensive defects and scars, particularly in the glans.

Tuberculosis is rare; occasionally, however, there do occur ulcers on the prepuce and the glans, usually as an accompaniment of tuberculosis of the urethra (p. 1454) or of severe urogenital tuberculosis (pages 1431 and 1368); in testicular tuberculosis the scrotum is likely to be involved. Wallart has described an interesting case of extensive clinically primary lupus of the scrotum and penis (see also Peters). An isolated penis tuberculosis may also develop, *e.g.*, from infection during the ritual circumcision in which the hemorrhage is stopped through sucking of the wound (Rose, lit., Wolff). According to Lindmann and Lehmann the tuberculosis is said to be rapidly distributed in the organism in such cases. See Kraus concerning infection of the penis through coitus per os.

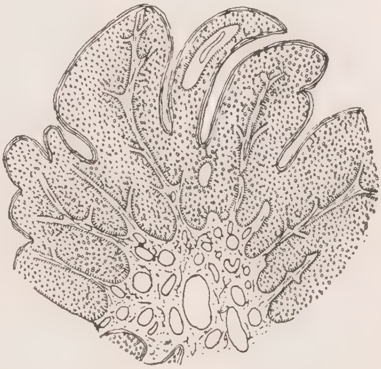


FIG. 796.—Acuminate condyloma of prepuce; core of enlarged and branching papilla with vessels and small cell infiltration; covered by epithelium; (about × 16).

Tumor-like Enlargements and Tumors of the Penis and Scrotum.—**Elephantiasis** occurs in the prepuce and scrotum, or the skin of the entire penis undergoes a monstrous hyperplasia.

Milder degrees occasionally follow extirpation or suppuration and destruction of the inguinal lymph nodes, or their infiltration by a malignant tumor. Recurring inflammation (erysipelas) may also lead to elephantiasis. The type due to the filaria sanguinis hominis of the tropics affects chiefly the scrotum (p. 210), which becomes twice the size of a man's head. Konjetzny described marked atypical epithelial overgrowth in the penis and scrotum—resembling, to a certain extent, an excessive condyloma acuminatum—which he believes is a reaction to primary elephantiasis. For the histology and etiology of elephantiasis, see under skin.

(*b*) The pointed condylomata (condylomata acuminata) are fibro-epitheliomas, the most frequent tumors of the penis (fig. 796). They are caused by the irritation of gonorrheal or tumor secretions, or even from the irritation of decomposed smegma in individuals predisposed to the condition (Saul). According to Unna's description, the process begins as a small button, which soon becomes lobed and then spreads in most cases to a cauliflower-like growth. The most important part is formed from overgrowth of the stratum germinativum. When they appear on the mucous membranes or the transitional places their color is usually red; on the skin they are white-yellow. They prefer the coronary sulcus and leave the glans free, but spread over the surface and then upward so rapidly and luxuriantly that they resemble papillary carcinomas; but in a papillary carcinoma the base of the tumor contains nests of carcinoma cells; in the condyloma it is infiltrated by round cells. In the condyloma there is no infiltrating growth. They do not, however, regress as do the cornifying verruca vulgaris; they do not metastasize, but may recur. For the histology, see under skin and under papillary fibroepitheliomas, p. 321. Phimosis may accompany these pointed condylomas.

Cutaneous horns, sometimes of considerable size, (as long as a finger), occur on the prepuce and scrotum, more rarely on the glans, but, in general, are quite rare. Pointed condylomas and seborrhoeic warts occasionally become the points of origin of a cutaneous horn.

A true cutaneous horn on section shows a softer medullary space, composed of the papillary vascular stalks; the epidermis covers this stalk in one or more thick layers of irregular, chaotic wavy cornified masses. Horny excrescences showing only many layers of evenly lamellated non-medullary tumors are called false cutaneous horns (Unna). See also keratosis and leukoplacia penis (lit. by Grundahl).

Carcinoma of the Penis.—The most frequent sites are in the inner leaf of the prepuce, along the ridge of the prepuce and the transition of the skin to mucosa, (the most frequent site, Englisch), on the glans; they are less common on the external layer of the prepuce. The type is usually that of a cornifying squamous epithelioma. Leukoplacia may be a forerunner (lit. Bohac, Iwasaki).

In leukoplacia penis there are dry chalky-white or bluish-white thickenings of the epithelium of irregular outline. It follows balanoposthitis; it is more frequent, however, in congenital or acquired phimosis (chronic irritation of the smegma?). Diagnostic difficulties arise in the differentiation of leukoplacia, the so-called acanthoma callosum, which consists chiefly of extensive hyperplasia of the epithelium (Baruch), papillary epitheliomas, and squamous epithelial carcinomas (Iwasaki, Betanges).

Carcinoma begins as a hardening, a nodule, a wart or ulcer and, in its further growth, may take on several forms. (*a*) The most frequent is the papillary carcinoma, often beginning as a small wart which rapidly enlarges but retains its papillary structure. The excrescences vary in the individual cases; they are thin or plump; a large, wet, sticky, cauliflower-like tumor may be formed, which grows upward from the skin, or in the phimosis carcinomas, in front of the opening of the prepuce or through it. The base of the tumor is infiltrated and hard; otherwise it is quite similar to a large pointed condyloma; these latter may be differentiated by the points mentioned on p. 1538, in addition to which they always leave the glans intact. But papillary carcinomas may possibly arise from condylomas (Klebs).

Carcinoma granulosum (Waldeyer) is a tumor in which the interstitial tissue is richly infiltrated by round cells, among which are many plasma cells and perhaps also Russel's hyalin bodies (Heigel; p. 301). The cornified, pale villi are sharply contrasted by their nuclear stains from the strongly stained interstitial tissue. (*b*) Infiltrating ulcerating carcinomas arise particularly on the prepuce; they produce extensive loss of substance with infiltration, and ulcers with overhanging edges (fig. 797). Kuttner (lit.) furthermore differentiates (*c*) a fairly uncommon type, a nonpapillary carcinoma, which arises from the glans, becomes nodular and may reach the size of a fist. The author has seen transitions of (*b*) to this form.

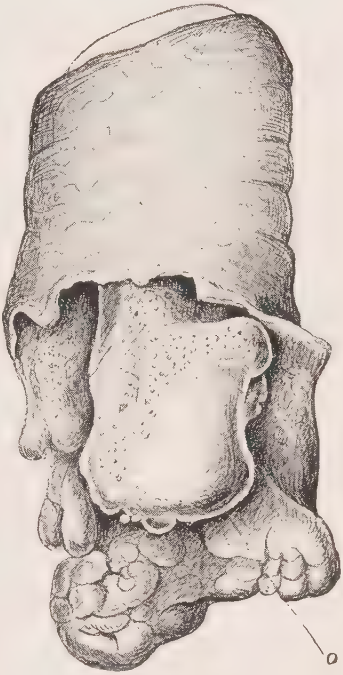


FIG. 797.—Infiltrating ulcerative carcinoma of penis; extensive destruction of prepuce, glans and shaft. Carcinomatous infiltration and edematous thickening of the anterior parts of the penis, still preserved; O, urethral opening; nat. size.

Carcinoma of the penis may infiltrate the urethra and along the lymph channels into the spaces of the corpora cavernosa. Not rarely, after creeping through the lymph vessels it breaks through the skin in higher situations. It may remain localized for a long time (see C. Kaufmann, Kuttner). The inguinal glands, and, according to Kuttner, the pelvic glands, are, as a rule, infiltrated relatively late; but softening, rupture, large ulcers with hard edges, and hemorrhages, even from the larger vessels of the thigh, may follow. In almost $\frac{1}{3}$ of the cases, carcinoma of the penis appears between the fiftieth and sixtieth year, and very rarely in earlier life (mistaken for syphilis!). Creite described a case occurring in a two year old child; among 616 cases, this was the only one under 20 years; but this case, according to W. H. Schultz, was not carcinoma, but hemangioendothelioma. It occurs most frequently in individuals with congenital phimosis (according to Barney in over 85%). Death occurs from cachexia. Metastases in internal organs are quite rare, but the author has seen a preparation (32 year old man) with metastases in the inguinal glands, skin, muscles, liver, lungs, heart.

Carcinoma of the skin of the scrotum occurs in the form of flat infiltrates which later ulcerate. Because of its etiological relationship to chronic irritation, as in chimney sweeps, paraffin and tar workers, this carcinoma is of particular interest.

The chimney sweep carcinoma is said to be due to the influence of coal dust. Paraffin and tar carcinomas follow the influence of irritating substances arising in the manufacture of coal tar and paraffin, which, over a period of years, mix with the perspiration and macerate the skin of the scrotum; there is produced the so-called "paraffin itch," and eczema (Kuntzel, lit.). Carcinomas of the extremities are also quite frequent in these occupations (v. Volkmann). Multiple primary carcinomas have also been described (Ehrlich, lit.). Yamagiwa produced carcinomas and also sarcomas by rubbing tar on rabbit's ears (see also Fibiger and Bang, Bloch and Dreifuss, Lipschutz).

Occasionally, a secondary carcinoma of the scrotum comes from the rectum (compare the observation of the author, p. 813; see also Kyrle).

Other Tumors.—On the penis occur: lipomas; angiomas; leiomyomas, perhaps multiple (Stavianicek), rarely sarcomas, easily mistaken for urethral carcinomas—they spread in the spaces of the corpora cavernosa, and have been described as endothelioma intravasculare (Maurer, Hildebrand, Colmers, lit.), but Borrmann doubts these diagnoses. Large round cell sarcomas, arising from the interstitial tissue of the corpora cavernosa, have also been found (see Heigel, lit.). Furthermore, there have been described melano-sarcomas, the so-called melanomas (Payr, Prigl, lit.), as well as congenital atheromas (dermoid—and epidermoid cysts) and cylindrical epithelial cysts, sometimes in the raphe penis (Fantl).

In the scrotum occur: lymphangiomas (Rosenberger, Bonamy and Dartigues); the author has examined a similar case, but these tumors are fairly rare. The same is true of cavernous hemangiomas; in a 12 year old boy the author saw a tumor as large as a chestnut; it had been present for 8 years. In another case, a tumor twice as large had appeared, accompanied by phleboliths as large as peas (Plum). Acquired atheromata include retention cysts of the skin follicles, the contents of which undergo calcification and ossification; they may number several dozen; dermoid cysts (see p. 576), and teratomas, which originate from fetal inclusions or an unfortunate twin, are rare (p. 623). For experimental sarcomas in animals, see above, under tar sarcomas.

Preputial Calculi.—According to Majocchi, these are (*a*) concretions of hardened masses of smegma of horny or waxy consistency. They are composed of hyalin or hornified epithelium, fat, mucus and a small amount of salts, mostly phosphates of calcium and ammonia. Dead bacteria may also be found in large numbers (Zahn; see under bacteria of the smegma, p. 1534). (*b*) True calculi are composed of urinary salts which arise autochthonously in the prepuce or come from above, and enlarge in this situation (balanocalculi); see illustrations by W. H. Schultze. In rarer cases, the phimosis may be markedly stretched to the size of a fist through the presence of a number of calculi. (*c*) Mixed forms, described by Zahn as brittle stones, are composed of a mixture of smegma and calcium salts from the urine.

DISEASES OF THE FEMALE GENITAL ORGANS

Ovary

Anatomy.—The ovary is an oblong body from 2.5 to 5 cm. long in the woman of child bearing age. Its weight is 5 to 7 grams. It is attached to the posterior surface of the broad ligament by the mesovarium, a small peritoneal reduplication. It is attached to the uterus behind and under the tube by the ovarian ligament, a small, partly muscular band which runs between the peritoneal leaves of the broad ligament. It is connected with the tube through the fimbria ovarica. The place where the blood and lymph vessels, and nerves enter from the broad ligament is called the hilum. The surface of the ovary is covered by a layer of low cylindrical epithelium with small intensively staining nuclei; these cells are always higher than those of the bordering peritoneum. As the embryology of the ovary shows, (see p. 1460), its surface, *i.e.*, the albuginea, has many epithelial cells which have lost their germinal epithelial character and are unable to develop further into germinal cells. It is therefore better to speak of surface epithelium, or as Walthard says, ovarian epithelium, rather than, as formerly, of germinal epithelium. In many animals the surface ovarian epithelium is ciliated; in humans this is also occasionally true (see p. 1567).

The stroma is of tough consistency and is laid down in several layers. For more details, see Hormann.

The outer layer (1) called the tunica albuginea, is composed of interlacing lamellae of connective tissue. This gradually blends into (2) the much broader cortical section or parenchymal layer or zona parenchymatosa; it encloses many follicles and is connected with (3) the medullary portion carrying many blood vessels as cork-screw-like arteries and wide veins. The vessels are accompanied by strands of smooth muscle. The transition from 2 to 3 is the subcortical region in which the principal development takes place of the so-called interstitial ovarian gland.

In the medullary part there are also rudimentary epithelial structures made up of germinal epithelium, the medullary strands or rays which are homologues of the straight tubules in the male; they may be found intertwined in a network. Between the medullary rays and the epoophoron in the hilum of the ovary is the rete ovarii which is the homologue of the rete testis; it undergoes its own differentiation into canals lined by a low epithelium; according to R. Meyer these structures are found in 85% of humans. Cysts and tubular adenomata may arise from them, see p. 1555. Also see under rete ovariae, p. 1569.

During pregnancy the connective tissue cells of the albuginea undergo an enlargement which has been called decidua-like (Schnell, Hormann and others, lit., see Risel, also consult decidual nodules under peritoneum). Such cells can also be found occasionally as individuals or in groups between the follicles of the cortical layer and in the medulla, particularly in the region of vessels in the latter case.

The epithelial sacs of varying sizes in the parenchymatous layer are called follicles; each one encloses an ovum. Most of the follicles are of microscopic size and in their outer layers toward the surface compose an arc shaped dome open only at the hilum. The development of the ovary up to the appearance of the primary or primitive follicles was discussed on pages 1460 and 1462. We no longer believe that in the third fetal month the germinal epithelium enters the connective tissue (mesodermal) stroma in the form of solid plugs (Nagel), *i.e.*, the so-called Pfluger's tubes, and that it then separates into cell groups and finally divides into isolated primitive follicles, (see p. 1462). R. Meyer speaks of an epithelial nucleus which comes from the same germinal epithelium from which the surface epithelium arises, *i.e.*, of an epithelial mass which constitutes the nucleus of the embryonal gland from which the real ovarian parenchyma and the rete arise. In the cortex, the parenchyma is broken up into "egg balls" in which ova are mixed; in these balls, follicles are differentiated—the primitive follicles—which are made up of one or, rarely, two or three ova, with surrounding indifferent epithelium of follicles or granulosa cells. Then the follicle cells increase in number and give rise to several layers of cubical cells, the so-called membrana granulosa or stratum granulosum. The ovum is embedded in this structure in an eccentric position; gradually there appears a space at first half moon in shape, and containing liquor folliculi, a product of the cells. The position now occupied by the ovum is prominent and is called cumulus oophorus; the cell body which is now called yolk shows a finely striated border zone, the zona pellucida, and contains a nucleus with polar bodies, *i.e.*, the germinal vesicle with germinal spot. On the outside, a connective tissue wall is built from the nonspecific connective tissue of the ovary and is called the theca folliculi, composed of the tunica fibrosa or externa and the tunica propria or interna, the latter soft, vascular and very rich in cells. The whole structure is a secondary or Graafian follicle. When the follicle becomes ripe, principally in the time between puberty and the climacterium, it forces itself toward the surface, and finally ruptures. The rupture of the follicle takes place about in the middle of the menstrual intermission, that is about the 9th to 14th day after the beginning of a period. See Strakosch in reference to the fate of the place of rupture of a follicle; it is first closed by fibrin and in nine to ten days by connective tissue. One or more Graafian follicles may rupture at any one time. The ovum, liquor folliculi, the cumulus oophorus, and some blood is emptied into the abdominal cavity (ovulation); under normal conditions the ovum is taken up by the tube. The empty follicle is transformed into a corpus luteum (the corpus luteum of menstruation). At first the empty cavity is filled with blood; occasionally, when there is no bleeding, it is filled with a slimy mass. The blood clots become deep red, and as pigment is formed, they become brown. According to R. Meyer and Hauswaldt, the corpus hemorrhagica arises only secondarily, either during or after the formation of the corpus luteum. Then there begins an active formation of lutein cells containing a yellow lipochrome, partly diffuse and partly in granules in the cells. These cells are supposed to originate from one of two places, either from the inner layer of the connective tissue theca, (Clark, Jankowski; lit., Hegar, and others), or, according to most other observers, (such as Sobotta, Pfannenstiel, R. Meter, R. Meyer-Ruge, Schröder, Miller), only from the follicle epithelium of the membrana granulosa, or, as still others believe, in reality from both, so that we may speak of theca and granulosa lutein cells (F. Cohn, Aschoff, Hauswaldt; lit., v. Franque). New capillaries arising from the theca grow between the cells, and thus there forms a structure microscopically similar to the adrenals, so that Wallart and R. Meyer speak of a glandular metamorphosis. The yellow lutein cell masses surround their contents like a ruffle-shaped membrane (fig. 798). This process is spoken of as the "blossoming of the corpus luteum" which begins on about the seventeenth day. If the ovum is destroyed, the specific granulosa part of the corpus luteum begins to disappear; the structure, however, persists until the beginning of menstruation or at least until the mucosa begins to take on its premenstrual character; then

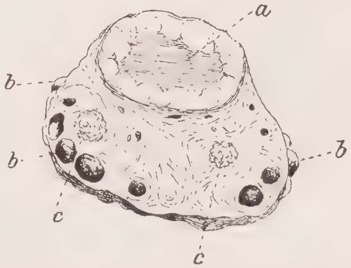


FIG. 798.—Section through ovary with large corpus luteum (a); the thick wavy margin was yellow; the homogenous stiff contents cloudy brown red; numerous small cysts (b) and two larger corpora fibrosa (c); 9/10 nat. size.

the phase of regression begins, in which there is much fatty degeneration, and in a few weeks, the corpus luteum has disappeared. The cavity is filled by granulation and later by fibrous tissue which finally shrinks into a hyalinized mass called the corpus fibrosum or albicans or candicans. The situations of former corpora lutea are often shown on the ovarian surface by shrunken areas, or by scars (lit. and details by Walter, Boshagen, K. Hegar). The whole is frequently called an endocrine corpus luteum gland. If the ovum which escapes from the follicle is impregnated by a spermatozoon (impregnation), the "blossoming" of the corpus luteum persists until the placenta and ovum have become strong enough to shift for themselves (see Schröder). This is the true corpus luteum of pregnancy; in this, all structures are much more prominently developed, and it remains much longer than the spurious corpus luteum of menstruation; as a means of differentiation, there does not occur a corpus hemorrhagica with blood pigments in the true corpus luteum, nor much fatty degeneration of the granulosa cells (lit. by Marcotty). Regression of the true corpus luteum begins in the middle of pregnancy, and is ended several months after the beginning of the puerperium. This regression is said to take place rather by way of necrosis than through fatty degeneration (Miller). The corpus may measure 1 to 1.5 cm. in diameter, (fig. 798), and even at the end of pregnancy is still quite large. According to Miller, certain "colloid droplets" are found in the lutein cells of the true corpus luteum, which cannot be demonstrated in that of menstruation; if there is much fat present in the cells, it is a sign of regression in the puerperium or that miscarriage has taken place, (see also Adachi).

According to the hypothesis of Born and L. Fraenkel, the corpus luteum is a gland of internal secretion built in the human every four weeks, and exercises the function of transmitting nutritional impulses to the uterus through which the latter is prevented from regressing into either the infantile or the senile stage; it also prepares the mucous membrane of the uterus to receive an impregnated ovum. If conception occurs it remains for a much longer time performing the same functions, but in heightened degree, because of the necessarily increased nutritive demands of the uterus. If impregnation does not take place, however, the hyperemia leads to menstruation, and the corpus luteum undergoes regressive changes. Menstruation is also said to be caused by the secretory activity of this body. It brings about, as L. Fraenkel says, the monthly cycle of hyperemia of the uterus which leads either to pregnancy or to menstruation. But, on the other hand, according to Villemin, and Seitz, (contrary, Mandl, Leopold and Rovano and R. Meyer), the ovum itself is said to play the dominant role in the cyclic changes in the sex organs by influencing the corpus luteum, and this in turn the uterine mucosa. This view is disputed by Birnbaum, Tschirdewahn (lit.) and others. In reference to the ovary and its internal secretion, see Birnbaum (lit.) and references by Munzer, Schröder, L. Fraenkel. Only the smallest minority of ova become ripe to the stage of the Graafian follicle; most of them—and there are said to be 10,000 in each ovary at birth, (see v. Hansemann)—are destroyed in the stage of primitive follicles. Others, after they have become partly ripe, are transformed into so-called atretic follicles, in children (lit. Benthin), as well as in adults. Follicle epithelium and ovum are destroyed, connective tissue surrounds the cavity as a hyalin band, (cystic or preliminary form, Wolz), later the connective tissue closes the cavity like a cork and obliterates the atrophic follicles. We can, however, often see around a ripening follicle, even if it later undergoes regression, that the elements of the theca interna increase in size and number to large polygonal lutein cells which contain doubly refracting lipoids (Adachi). But the individual atretic follicles from the theca interna coalesce to an epitheloid tissue spread out in the subcortical region. This lutein cell tissue comprises the so-called interstitial ovarian gland, particularly well developed in certain animals (rodents, see Bouin and Limon). In humans, this growth is inconstant (L. Fraenkel and Schaeffer), is greatest during childhood until puberty, and particularly marked during pregnancy, during which all structures containing lutein cells or their remnants, *i.e.*, the scars of follicles, atretic follicles, etc., undergo hypertrophy (Wallart, lit., Seitz, Wolz, see opposed Ganfini). Their significance and their independence are debatable. Schröder, with whom R. Meyer agrees, is entirely opposed to the opinion that the interstitial ovarian gland is an independent structure. The function of the latter in the human ovary is said by them to be related to the follicles, particularly to the theca cells, which in adults are found only sporadically in the interstitial tissue, as remnants of a follicle which has undergone regression. For purposes of internal secretion only two structures remain in the parenchyma, viz., the ovum and the follicle cells. As long as the ovum remains in the follicle the internal secretory activity is confined to this structure; when the ovum is cast off, the corpus luteum takes over its function, but in such a way that the follicular epithelium, as well as the granulosa cells, are nothing but assistants to the ovum which belongs to them. The ovum and the follicle cells are the parts of the parenchyma which determine sexual characters, while the interstitial ovarian gland, or the puberty gland (Steinach), has an influence on the development of secondary sex characteristics (Stieve). See lit. in appendix in reference to ovarian function. See Ancel and Bouin in reference to the "endocrine myometrial gland" of pregnant rabbits, which are cell masses in the inner circular muscle bands of the uterus and which arise from the placenta (L. Fraenkel), or from connective tissue Muraoka, lit.).

Lymph Vessels. Larger vessels are found only in the medulla of the ovary (lit. Kroemer). They empty into the lumbar zone and anastomose with a network passing from the body of the uterus along the ovarian ligament to the hilum of the ovary, and with tubular channels which empty into the lumbar zone (Bruhn, Polano).

In the ovary of a fifty-five year old woman, Bucura saw masses of chromaffin cells (see p. 1277), and between them typical unipolar ganglion cells connected with nerves. (For the nerves of the ovary, see Wallart; for their endings, see Akagi. See Wallart concerning the smooth muscle of the ovary which is subserous and intervascular and which becomes hyperplastic and hypertrophic during pregnancy and perhaps has an important regulatory influence on the internal secretion of the organ.)

Senile Involution.—Senile ovaries undergo atrophy; ova and follicles disappear and the fibrous portion of the cortex predominates; the organ becomes hard, nodular and shrunken, often with a convoluted or furrowed surface relief. (Concerning formation of furrows on the ovarian surface, see Bien.) It usually contains corpora fibrosa, often in large numbers. The arteries, particularly those in the medulla and hilum, are uniformly and almost without exception thickened in the intima, are often hyalinized, and occasionally calcified. Quite frequently sunken areas or snared portions of ovarian epithelium can be observed in the stroma (see under the development of cysts, p. 1566). Psammoma bodies are often encountered. But Sohma described a wide-spread change in the ovarian vessels as a menstrual ovulation sclerosis which may be compared to those changes in the uterine vessels which result from menstruation and pregnancy and which are entirely independent of senile changes. Haendly has described the atrophic tendency of x-ray treatments, after which there is destruction of the entire follicle apparatus, and at first an increase, but later, disappearance of the so-called interstitial gland.

Malposition in Hernias (the so-called ovarioceles). An ovary may be misplaced (*a*) in a congenital hernial sac, particularly in an inguinal hernia (p. 729). The hernia may follow the round ligament into the labia majora (hernia labialis, p. 734), and is usually reducible; (*b*) in acquired hernial sacs, usually femoral, in which the ovary and its tube are generally irreducible because of adhesions in the sac with other structures such as intestines or great omentum, which often pull the ovary into the sac. Other hernias such as ischiatic, obturator, umbilical and abdominal, (pages 734 and 735), also occasionally contain an ovary.

Supernumerary Ovaries.—Chiari distinguishes (*A*) accessory ovaries in which the separated parts appear as appendages; (*B*) bi- or pleural ovaries which arise very early or during the very first developmental processes; and (*C*) the rare numerical excesses on one or both sides, so that, instead of two ovaries being built from coelom epithelium, many ovaries arise, with perhaps many tubes. Various kinds of tumors such as embryomas, dermoid cysts, ordinary cysts and so on, have arisen from these multiple ovaries. (For lit., see Stolz, Winternitz and Henke, Essen-Moeller, Engstrom, Tsuge, Monch.)

Transplantation of Ovaries.—Homoioplastic, *i.e.*, transplantation from one to another individual of the same species, showed in experiments with mammals, (Tschernischoff), a disappearance of the Graafian follicles and later, after five and one-half months, disappearance of the primordial follicles. Autoplastic transplantation, (reimplantation), in humans, showed ripening of the follicles and development of corpora lutea and albicans; in animals, even pregnancy occurred (Pankow, Higuchi). Even five years after autoplastic transplantation, Unterberger saw regular menstrual periods. Steinach transplanted ovaries into previously castrated male young rats and guinea pigs; in his cases only the so-called interstitial glands remained, and these males gradually took on both the bodily and psychical attributes of females.

Circulatory Disturbances.—Hyperemia of the ovaries is related to congestion in the other sex organs during menstruation, pregnancy, coitus and so forth. Edema of the normal ovary through torsion of the pedicle may reach an excessive degree and lead to outstanding enlargement of the organ. Hemorrhages occur in the follicles, the yellow bodies, or in the stroma. In relation to the consequences of larger hemorrhages into the peritoneal cavity, see under peritoneum, p. 861.

The causes of hemorrhage may be as follows: peritonitis, in which, in acute fulminating cases, many hemorrhages are found in the outer layers of the ovaries; acute infectious diseases such as cholera, typhus, influenza and others; puerperal infection; intoxications particularly with phosphorus; the hemorrhagic diatheses such as scurvy; excessive congestive hyperemia, menstruation, coitus; finally there are rare torsions, and more frequent congestive hemorrhages when the outflow of blood through the veins of the broad ligament is disturbed, *e.g.*, by tumors, fixed retroflexions and other such conditions (lit. see Cantoni, Strassmann).

In follicular hemorrhages the follicles become as large as hazel nuts or walnuts or larger. Through pigment changes, they become like a corpus luteum. The hemorrhage may be merely an increase of the normal menstruation hyperemia, but when more follicles are involved, it becomes of pathological significance. These are spoken of as hematomas (see Savage), but they may also arise via hemorrhages into corpus luteum cysts (see p. 1552). The consequences are, (*A*) disappearance of the ovum without rupture of the follicle; the contents are absorbed, the site may shrink to a pigmented scar or remain as a cyst. (*B*) The follicles rupture, blood flows into the peritoneal cavity, (see p. 861 with lit.), peritonitis or death from hemorrhage follows, or there develops a retro-uterine hematocele (see Lunzer, Reinhard, lit.).

Interstitial hemorrhages (hematoma of the ovary) are rarer; they may be small, single or multiple, and even as large as a child's head. In diffuse hemorrhage, the ovary looks like a blood-soaked sponge (Olshausen). The results are: small hemorrhages may be absorbed and leave no trace; larger ones leave hemosiderin behind. After a large diffuse hemorrhage the ovary may shrink or become a cystic sac. See p. 1546 in relation to the menstrual and ovulation sclerosis of the vessels in the cortex and in the cortical border.

Inflammation of the Ovaries. *Oophoritis.*—Mostly occur in connection with inflammatory processes in the uterus, the tubes (puerperal, gonorrheal) and the peritoneum.

In follicular parenchymatous oophoritis, which, according to Slavjansky, occurs in typhoid fever, scarlet fever, cholera, recurrent fever and phosphorus poisoning, there are degenerative changes such as cloudy swelling and fatty degeneration in the epithelial parts of the ovary; disappearance of the diseased follicles or shrinking of the entire organ follows, perhaps also cystic changes.

In acute exudative inflammation, the organ becomes enlarged in a very short time from the exudation of fluid into the interstitial tissue. As a rule, the follicles also are changed. Serous oophoritis is the mild degree of this inflammation, but the ovary may show small hemorrhagic spots (oophoritis hemorrhagica). Serous readily becomes purulent oophoritis. If the interstitial tissue is diffusely infiltrated with a seropurulent fluid (phlegmonous oophoritis), the organ as a whole becomes much larger, and may exude pus from its surface. When the infiltrated tissue softens, the section surface appears greenish yellow, and poorly outlined abscesses gradually develop. If, on the other hand, a follicle suppurates, a rounded follicular abscess results.

An ovarian abscess quite frequently begins in a suppurating corpus luteum. The infection at first attacks a recently ruptured follicle, is, therefore, as a rule, solitary, and arises mostly from the tube or from the peritoneum. The internal surfaces of corpus luteum abscesses are granular as though strewn with frog's spawn, very much folded, and plicated; at first they are no larger than a normal yellow corpus. In this stage they are still characterized by many lutein cells. As the abscess enlarges through liquefaction of the tissue, larger cavities appear with granulating walls in which lutein cells are absent, but in which large fat-containing granulation cells (pseudoxanthoma cells) can be found. (Lit. Langer, Orthmann, Kehrer, R. Meyer and others; for the differential diagnostic points see the end of this section, p. 1550.)

Healed ovarian abscesses may be covered by epithelium from the surface cells, and thus perhaps become cystic (R. Meyer).

Suppurative inflammation may be mixed with hemorrhage into the tissues, and the condition may at times become a phlegmonous oophoritis, particularly in puerperal infections, but also together with salpingitis, and, on the right side, with appendicitis (p. 838). In necrotic septic oophoritis, as in puerperal sepsis, the organ may liquefy into a smeary necrotic pulp. Peritonitis is seldom absent.

Wertheim first called attention to pure gonorrheal abscesses without the admixture of streptococcus infection. They are quite common. In the exudate are many lymphocytic and plasma cells (Watjen). The most severe degrees of oophoritis are found in connection with puerperal infection, others may be metastatic, others may follow operative procedures in this neighborhood.

The route by which inflammation reaches the ovary may often be followed quite clearly. (*A*) Oophoritis lymphangitica. Lymphangitis spreads from the uterus through the broad ligament into the hilus of the ovary, and even in the interior of the softened organ, when the yellow green stripes indicate the paths of lymph channels. (*B*) Oophoritis thrombophlebitis. Inflammation follows the veins. Quite frequently suppurative oophoritis is secondary to suppurative peritonitis or salpingitis; the form taken may be that of a diffuse phlegmon or a suppuration of follicles, of corpus luteum cysts, or of corpora lutea.

Even if ovarian abscesses become chronic, they may, after weeks or even after years, rupture into the peritoneal cavity with peritonitis as the result, or into the intestines particularly the sigmoid flexure, into the vagina, or through the abdominal wall to the outside. An old abscess is surrounded by a fibrous capsule with a tough wall and is often very tightly adherent to neighboring organs, (perioophoritis adhesiva). The abscesses may be as large as a fist or even a man's head. In smaller abscesses the pus thickens and perhaps calcifies. Perioophoritis is often found with ectopic formation of deciduae in which the adhesions may also take part (R. Meyer). The autopsy findings are very complicated: perhaps there is an abscess as large as a fist filled with fluid pus on one side, or in the midline the abscess wall is thick and often tightly adherent in Douglas's cul de sac, or to the posterior wall of the uterus. Since all the organs are so tightly bound to each other, it is sometimes difficult to determine the exact nature of the trouble. It may be mistaken for a pyosalpinx or a suppurating cyst. Finally, the abscess may belong to both the tube and ovary, (tube-ovarian abscess), if the tube and ovary had previously grown together. Microscopic examination may differentiate; the most important findings are corpora albicans, but a suppurating corpus luteum or so-called lutein abscess may cause confusion. There occur, as Miller remarks, pus cavities which belong to the tube or to the ovary and which are surrounded by circular yellow borders, and so may mimic lutein abscesses or abscesses arising in the corpora lutea (see p. 1548); this border is composed of a granulation tissue, rich in leucocytes containing many fat droplets which determine the yellow color. Even microscopically in a stained preparation, these cells are not easily differentiated from lutein cells.

Chronic Oophoritis. This is often a further stage of an acute puerperal or non-puerperal oophoritis, and is characterized by connective tissue induration. It may, however, begin insidiously, and progress over long periods of time. It is often seen in relation to chronic catarrhal endometritis, whether gonorrheal or not, which condition is often found with disturbances, irregularity, and pain at the menstrual periods; furthermore it occurs, particularly in cases in which the inflammation begins on the surface of the ovary, as a perioophoritis, as in chronic pelvic peritonitis, in which case the induration is found in the cortical layers (oophoritis corticalis). In the latter case, the ovary may become enlarged and painful, the surface is smooth, of milky white color, and thickened as though covered with icing, or it may be embedded in adhesions. If the oophoritis follows puerperal infection or uterine catarrh, the organ may become as large as a hen's egg or larger, and is tough and fibrous, while the follicles gradually disappear. As an end result of a violent acute oophoritis, the ovary becomes nodular and hard, deep scars and folds appear so that the organ shrinks to the size of a bean (ovarium gyratum) with a peanut-like surface; fibrous tissue is established, in which many, if not most, of the primary follicles disappear; corpora candicans and small cysts are often very numerous.

Hoffmann believes that the picture of chronic oophoritis can be brought about by an overstimulation of the normal ovarian structure, in the sense that an abnormally increased development of the stroma, and perhaps of the follicles also, occurs because of circumstances in which active hyperemia is present; chronic oophoritis would then be, properly, chronic hyperemia of the ovary.

Adhesive perioophoritis is often coincident with oophoritis. The ovary is hidden in adhesions which bind it to neighboring organs such as the tube, the uterus, the rectum.

R. Meyer calls attention to well developed epithelial gland-like growths in the adhesions about the ovary, particularly in those to the tube.

Epithelium may also be snared off in the inflamed ovary, and give rise to cysts.

According to Hegar and others, a chronic inflammation which involves chiefly the surface of the ovary, not rarely leads to so-called follicular or small-cystic degeneration. The surface follicles, after destruction of the epithelium and ova, are changed into cysts as large as the heads of pins or peas with clear contents, (fig. 798). This is usually accompanied by a well developed thickening of the cortex. While Bulius, Stratz and others accept Hegar's opinion, Nagel believes the formation of these small cysts is the effect of a previous too early ripening of the follicles. Schultz suggests a reflex overstimulation of the follicles; R. Meyer considers the designation "cyst" altogether wrong. Pfannenstiel speaks of chronic oophoritis brought about by oft repeated hyperemia. Bartel and Herrmann, on the contrary, say that such ovaries characterized by large size and form anomalies such as smooth surfaces, connective tissue hyperplasias, and disturbances of the follicular apparatus, are not the result of an oophoritis, but are the expression of a hypoplastic constitutional developmental anomaly. The condition appears in the first years after puberty and later, but such have been seen in children and even in the new-born. Forgues and Mabouillot relate typical, often profuse, hemorrhages from the uterus, to small-cystic degeneration of the ovaries; (see also Adler, who believes they are the opposite in this respect to a corpus luteum cyst); still others dispute these conceptions, see Schickele and Keller. According to v. Kahlden similar pictures come from adenoma formation from the germinal epithelium. But in contradistinction to small-cystic degeneration, this cystic adenoma is seen particularly in older individuals and is frequently accompanied by perioophoritis. Walthard confirms this statement, but believes that the matrix of the adenoma-like tubes are very small groups of indifferent cells from the surface epithelium, which appeared in excess numbers during the development of the ovary, and failed to reach their final functional position; some remained connected with the surface epithelium, others separated from it, and came to repose in the layers of the zona parenchymatosa. The finding of parts of the primitive kidney has been related to many cases of small-cystic degeneration, or cases similar to this (from v. Babo; see p. 1567). Small-cystic degeneration of the follicles can also occur from hydrops in torsion of the pedicle of the ovary (Geyl).

Infectious Granulomata.—Tuberculosis is uncommon. It is questionable if it ever occurs as a primary lesion (v. Franque), and only by careful post mortem investigation can the question be settled in any individual case. Usually it is found with tuberculous salpingitis or uterine tuberculosis, in the form of small nodules in the ovarian tissue which undergo caseation; the ovaries may enlarge to the size of a fist and give the impression of a solid malignant tumor (v. Franque). Usually there is a coincident tuberculosis of the peritoneum or of the tube, from which the disease enters the surface of the ovary. In such cases, there are microscopic tubercles in the cortical layers of a seemingly healthy ovary, occasionally also in the walls of a corpus luteum. In the latter condition, Cohn believes tubercle bacilli enter the follicles from the surface of the ovary through the place of rupture. The disease may, however, be hematogenous in origin, although rarely, because, in general, the ovary is quite resistant to tuberculosis (see Kundrat). Occasionally tuberculous infection is observed in ovarian cysts (p. 1565).

Secondary **actinomycosis** appears in the form of a spongy tissue, the meshes filled with a granular pus; the peritoneum as well is practically always involved. Bostroem, in intestinal actinomycosis, found the condition arising mostly from the appendix, and from there it spread to the uterine adnexa. (Lit. see Rosenstein, Schlagenhaufer, Schiller, Wunschik.) Primary ovarian actinomycosis is discussed by Tonnies. Leukemic infiltration appears diffusely or in nodules.

Simple Cysts and Tumors of the Ovaries

Small-cystic degeneration in which the cysts are as large as a ripe follicle and no larger, has been discussed on p. 1551. Corpus luteum cysts (Rokitansky) usually contain serum and no epithelium; they are not true neoplasms but arise perhaps from corpora lutea or from the accumulation of fluid in a corpora lutea fibrosum; the inner surface is made of layers easily pulled apart, and consisting of fibrin, tender connective tissue and innumerable capillaries, between which are large rounded pigment-containing cells (lutein cells) and leukocytes (Nagel, Eug. Fraenkel). If they contain a few epithelial cells (granulosa lutein cells), an uncommon finding, these develop from remains of granulosa epithelial cells, and are thus true follicle cysts (Eug. Fraenkel, Orthmann and Martin, Grouzdew). The authors who believe the lutein cells arise from two situations, also postulate ordinary lutein cell cysts arising from atretic follicles and lined by theca lutein cells and not by granulosa lutein cells (Forgues and Massabuan). The thin-walled corpus luteum cysts, which may reach the size of a small apple, have been known to rupture during bimanual examination. These are said to inhibit the menstrual bleeding (Halban). Ruptured corpus luteum cysts may start a retrouterine hematocele (lit. Lunzer). Garkisch discusses tuberculous corpus luteum cysts. For their frequency in tubal pregnancy, see L. Fraenkel.

Stoeckel, E. Runge, Pick (lit.), Krebs and others describe in chorion epitheliomatous tumors of the uterus and in hydatidiform moles, a more or less frequent, multiple, so-called lutein cyst formation, seldom very large (man's head), which often changes the ovaries bilaterally into multilocular cysts and similar structures (lutein pseudocysts). The thin-walled cysts shining through the nodular surface of the ovaries contain water and sometimes bloody fluid. The inner lining is made up of a layer of lutein cells of varying width; these cysts seldom grow very large, and may be surrounded by a connective tissue layer (theca externa). But there have also been many cases observed in connection with hydatidiform mole and malignant chorion epitheliomas in which the ovaries have been little or not at all enlarged, indeed have sometimes been smaller than normal. The author saw such a case in a 46 year old woman with a hydatidiform mole. In addition to this, mass production of lutein cells has been found in every normal pregnancy and often also in the non-pregnant; finally it is found even without atretic or cystic dilated follicles. On the other hand, ovaries without microscopic overproduction of lutein tissue (Jaffe) may also be present with malignant chorion epitheliomata. It follows from this that it is neither a specific nor yet a diagnostic finding in hydatidiform mole and chorion epithelioma (Wallart, lit., Seitz, Risel), even though it is so stated over and over again (Fischer). But spontaneous regression of cysts from the size of fists to children's heads has been observed after removal of a hydatidiform mole (L. Fraenkel, lit., Santi, Ballerini and others). From this the conclusion has been drawn that the mole originally brought forth these changes in the ovary. Conversely, it has also been concluded that an excess production of lutein cells brings about the degeneration of the chorion to a hydatidiform mole (Jaffe). Penkert (lit.,) is, however, of the opinion that a hydatidiform mole and a chorion epithelioma are not necessarily primary, nor are the changes in the ovary necessarily secondary, or vice versa, but that both of these changes are brought about by a hypothetic hormone.

Follicular Hydrops.—(Follicular cyst, or hydrops folliculi Graafii.) If a Graafian follicle does not rupture, it may, in time, become a cyst, through increase of the transudate; its wall, often in two layers from the theca folliculi, is usually lined by a simple low cylindrical follicle epithelium, but this may be entirely lacking. Its content is a thin serum-like non-coagulable fluid, usually water clear, but occasionally stained with blood or pigment. Occasionally, in the small cysts, ova may still be found, but usually, in the larger ones, they have disappeared. In a case of Neumann, a cyst as large as a head is said to have contained thousands of ova; but this was obviously a neoplastic process, and not a simple hydrops, provided, of course, that the picture was not misinterpreted, and that the so-called ova were not in reality large vacuolated cells from some other source, (see pages 1566 and 1567). The cysts are often bilateral, single or multiple; a single cyst may be as large as a fist, in occasional cases (according to Olshausen) the size of a man's head; v. Franque speaks of them as simple serous cysts. When the separating walls rupture or disappear, larger cysts form by confluence. The ovarian tissue in the presence of these larger hydropic follicles is mostly fibrous and atrophic, and pushed into the periphery; ovum-containing follicles may still be found here and there. At times there are found in girls past the age of puberty, ovaries full of cysts, usually no larger than cherries, which shine through the surface as bluish structures. v. Franque has described a cystic hydropic follicle with torsion of the pedicle in a new born infant.

While most authors believe there is an inflammatory exudative process concerned in these follicular cysts, because definite adhesions in the neighborhood and catarrhal changes in the endometrium are often present, Pfannenstiel believes that only those without epithelium are follicle cysts, and that all others are new growths (simple serous cysts). v. Kahlden is of the opinion that many adenomatous structures arising from snared off germinal epithelium arise from the small cystic form as described on p. 1551, and furthermore, that the ova as found by others are in reality incompletely differentiated cellular ovum-like structures.

See p. 1596 concerning the relation of follicular cysts to tubo-ovarian cysts.

Small Cysts on and in the Ovaries, on the Tubes and Broad Ligaments.—Walthard has shown that there are masses of germinal cells of surface epithelium (see p. 1551), as well as squamous, ciliated and goblet cells congenitally present in the ovarian epithelium and the stroma. He used these findings for a very plausible and simple explanation of the genesis of the many small-cystic tubes and cell conglomerations about which there has been such difference of opinion, and which are found, not only on and in the ovaries, (Walthard's work is particularly concerned with these), but also in similar guise and ofttimes coincidently on the tubes, in the broad ligaments, particularly on their posterior surfaces, in the mesovarium, and on the ala vespertilionis, (see also under cysts of the ovaries, pp. 1566 and 1567). These cell masses, tubules and cysts are possibly in part results of a growth, *i.e.*, a true neoplastic process, of peritoneal epithelium of the same general nature as the so-called germinal epithelium of the ovarian surface (Pick), in which the cylindrical and flat cubical cell is transformed into the ciliated cell. In their growth they give rise not only to cysts, but also to ciliated adeno-cysts. These small rudimentary structures are, therefore, similar in principle to the large cylindrical ciliated epithelial cysts of the ovary. Schickele believes, with Fabricius, that the large majority come from germinal epithelium which proliferates under the stimulus of an inflammatory condition in the ovaries, tubes or broad ligaments. He describes his "germinal epithelial cysts" as being superficial, directly under the serosa, covered with a thin fibrous wall, and lined with layers of pavement epithelium. Finally, Fitting believes that nodules in the broad ligaments and on the tubes arise, at least in part, from embryonally misplaced germinal epithelium. v. Franque described masses of pavement epithelium in layers on the tubes and on the under surface of the mes-ovarium which he believed came from peritoneal epithelium (peritoneal epithelial cysts). R. Meyer believed that subserous, sometimes cyst-forming, and very variable kinds of epithelial tissue in the tubes and broad ligaments was caused by an inflammatory growth of the surface ovarian epithelium and he says, but, of course, his opinion has been disproved by the findings of Walthard, that they have not been found on the ovary. Walthard never found any evidences of inflammation. Incidently it might be mentioned that Rossa and Pick believe that cysts and cell conglomerations in a state of regressive metamorphosis, or in younger stages, are accessory adrenal glands; this idea, however, has been vigorously opposed by Schickele and R. Meyer. Other cysts in the broad ligament and in the ovary (in the hilum) are epoophoron cysts (see p. 1569).

Tumors of the Ovaries. Benign Epithelial Tumors.—The most common benign epithelial tumor of the ovaries is the cystic adenoma, which reaches various sizes and is uni- or bilateral.

Occasionally, cysts weighing more than 50 kilos have been observed. In a cyst found at autopsy by the author, (fig. 799), the weight of the fluid contents was 93 pounds (lit. Idaszewski, Pfahler, Zacharias). See Rubsamen in relation to the changes in the position of the thoracic organs. Cysts have often been found in children (lit. Kelly, Wiel, Mac Gillivray).

Pure solid adenomas are very rare (Glockner); Pick identified tubular adenomas of the ovaries with masses of similar appearance in the testes of male pseudohermaphrodites (see p. 1498), and believed that their starting point is from a very small inclusion of testicular tissue in the ovaries. R. Meyer, who has described a "tubular carcinomatous adenoma" of the ovaries, can agree with Pick's opinion of a partial glandular hermaphrodite only with reserve; he considers it more likely that these adenomas arise from the rudimentary homologues of male parts (rete and tubuli recti), normally existing in the hilum and medulla of the ovaries, (see p. 1542).

The tumor may have one or many compartments. The multilocular cysts are much more common than the unilocular through confluence of many cysts; in unilocular cysts, microscopic ones can usually be found in the wall. The compartments are, as a rule, of unequal size. Often there is a main chamber which has many smaller nodular cysts jutting into it. According to their external appearance they are differentiated into:

A. **Simple cyst adenomas or glandular cyst adenomas,** mostly multilocular. The inner wall is generally lined by a flat palisade-like cylindrical epithelium. The contents are usually sticky, pseudomucinous (pseudomucinous cysts). The tumor may reach an enormous size.

B. **Papilliferous Cyst Adenoma.**—This tumor also is usually multilocular, but its inner surface contains many branching papillae covered by a layer of low cylindrical ciliated epithelium (ciliated epithelial cysts). The contents are serous. Ordinarily the tumors are as large as a child's or a man's head; the larger the cyst, the fewer the internal papillary growths.

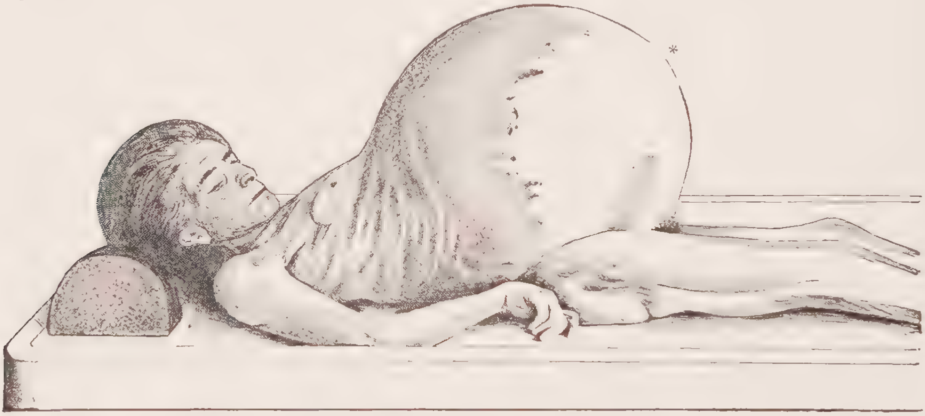


FIG. 799.—Enormous simple multilocular cystadenoma of r. ovary of woman 59 years old; advanced marasmus (tumor weighed 163 lb.). Death from intestinal obstruction; body length, 139 cms. Circumference of body 143 cms. The thin gray white opalescent stringy fluid of the cystoma (46 l.) weighed 93 lb.; position of diaphragm, l. 1 intercostal space, r. 4 rib. *Level of umbilicus.

C. **The solid tumor** known as the surface epithelial papilloma of the ovary is closely related to the papilliferous adenoma. There is, also, a simple serous cyst, lined by simple flat epithelium without papillae; if large it may be free of epithelial cells and of pseudomucin. In such a tumor, however, even in one as large as a child's or man's head, the microscope calls attention to isolated papillary formations, thus showing its actual relationship to a papilliferous cyst adenoma (Pfannenstiel). v. Franque separates the simple serous cysts from cystic new growths in the narrower sense and places them in the same category as the follicular cysts (p. 1553); see also R. Meyer lit.

The rare grape-like ovarian cysts (Olshausen) have been described as serous cysts. They are unilateral, usually leave the ovary intact, and for their genesis, authors postulate a third ovary, or a misplaced nodular ovarian anlage, or, if it comes from the ovary, an epithelial fibromatous mass which had been snared off. In the cases of G. Klein and Treber, the conditions were serous cyst adenomas which, on account of the accumulation of fluid, caused a transparent myxomatous swelling of the tissue and reminded them of hydatidiform moles. The author saw such a roughly nodular tumor larger than a fist arising in an ovary; the various compartments held a sticky fluid separated by thin walls; many cavities were confluent and the whole resembled, even microscopically, the ordinary pseudomucinous ovarian cysts. These cases are rare. Hirschenhauser (lit.) has recently described a similar case of grape-like pseudomucinous cyst which he believes arose on a teratomatous basis (see also Mulier, Bolaffio).

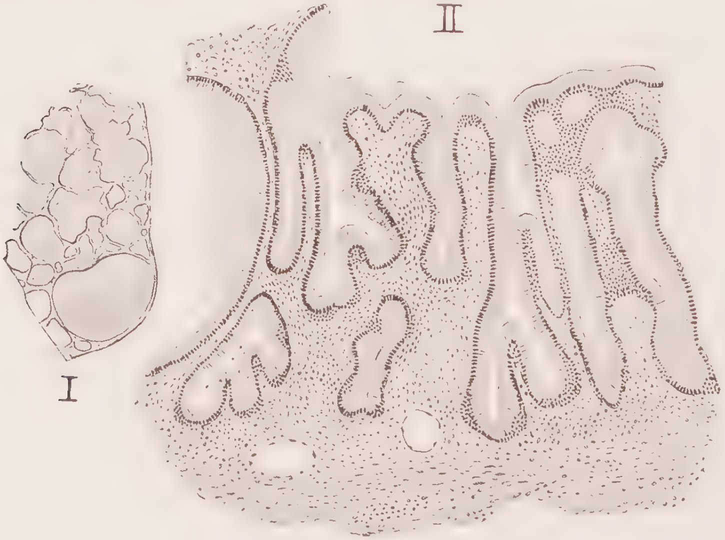
There are also other differentiations of epithelial benign ovarian tumors. Thus R. Meyer differentiates under the word cyst:

A. Blastoma cilioepitheliale serosum.
  1. Adenomatosum, or, better, adenoides.
  2. Papillare.
  3. Cysticum.

B. Blastoma epitheliale pseudomucinosum.
  1. Adenomatosum.
  2. Pseudo-papillare.
  3. Cysticum.

Simple Cyst Adenoma.—This is the commonest form of cystic ovarian tumor and is quite variable in its macroscopic appearance. The tumors may be very small or very large. As long as the tumor does not reach an excessive size, the outer surface is usually ridged; if very large, it is more rounded. Usually the whole tumor, as seen on section, is made up of one or more principal cysts, the smaller ones jutting into the larger ones. Where there are many small, fairly uniform cysts, the consistency is tougher and the section surface is meshed. The wall of large older sacs is tough and fibrous; of younger ones, it is thin and composed of soft, richly cellular mucoid tissue. The inner walls are generally smooth and lined by a single layer of cylindrical epithelium. The cells are high, similar to intestinal epithelium; they are homogeneous in their peripheral part, but in the neighborhood of the nucleus, usually situated at the base, they are somewhat granular. In old large sacs the lining epithelium may be flattened. Ciliated epithelium is also said to be present occasionally. The tube may be stretched and hypertrophic.

The cyst contents are of varying consistency, usually thin and sticky, seldom thick, but occasionally can be cut with a knife; in other cases it may be stringy like mucus or almost serous. The content of pseudomucin is correspondingly variable. The color also varies; sometimes it is glassy or water clear, often opalescent; more rarely it is bloody or cloudy, like pus; at other times it is cloudy gray, or cloudy yellow or red from blood pigment, or brown and opaque. It is common to find cloudy yellow pus and flakes in the viscid fluid, and microscopically, fatty and colloid degenerated epithelial cells and leucocytes. The fluid may be secreted by the epithelial cells, whereupon goblet or rounded cells with mucoid globules can be seen. The fluid is also in part a product of degeneration of epithelial cells and leucocytes, and furthermore a transudation of albuminous fluid from out of vessel walls. In passive congestion the portion due to transudate may be quite considerable.



Figs. 800 and 801.—I. Piece of a simple multilocular cystadenoma of ovary with thick gelatinous contents; nat. size. II. Simple multilocular cystadenoma of ovary; section from wall of large cyst. Duct-like structures grow downward and glandular formations present deep in the stroma; cylindrical epithelium with nuclei near the base line; here and there nuclei are cut flat. (High power.)

Very frequently, small depressions and uneven areas are found in the wall of the cyst even with the naked eye; microscopically they prove to be glandular spaces with the outlets obstructed, representing the adenomatous beginning of the very youngest cysts. These enlarge through addition of fluid and disappearance of septa, so that many jut into the neighboring cysts. New cysts are constantly being made by the snaring off of new glandular formations in the walls, and stretching from increasing contents. Smaller cysts by disappearance of their walls become confluent and thus larger cysts arise. While the walls in general are sufficiently strong to give the entire polycystic tumor considerable resistance against rupture, nevertheless, some are very easily torn. These with their tendency to spontaneous rupture have been called "jelly tumors" by

Gebhard. Once in a while, the small glandular cystic structures are so numerous that they give the impression of solid tissue (fig. 803) and the inexperienced observer often will give as his opinion that it is a malignant change. On closer examination, in the white or yellow medullary, finely granular tissue are found irregular cystic alveolar spaces filled with a viscid grayish white fluid.

Microscopically, in the latter places, are many plica and folds similar to papillae, arising from the cyst wall and jutting into the cystic spaces. But these are, as Waldeyer said, and as can be shown in serial sections, (Saxer), usually not papillary growths which filled the original spaces, but only stumps and excrescences of septa and so on. Glockner believes it is characteristic of these pseudo-papillary cysts to have partitions of various thicknesses between the cysts. This coincides with our experience. At other times, microscopic alveolar pictures are very prominent, while the pseudo-papillary pictures are lacking, as shown in fig. 803. The contents may occasionally be very fatty, granular and not homogeneous like pseudomucin.

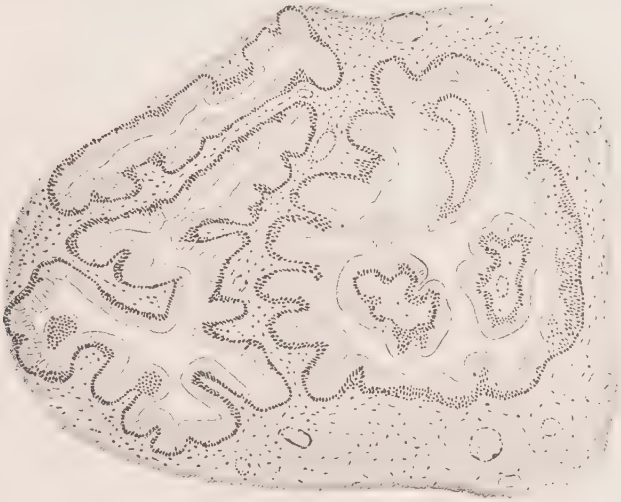


FIG. 802.—Denser area with true formation of papillae from a multilocular glandular cystadenoma the size of a man's head, and of the usual appearance; girl 19 years old, supposed presence for 9 months, with greater enlargement within the last few months, operative specimen. Both papillae in cross section very plain, free in the lumen of the hollow space to the right; in same section a surface cut through epithelium of a papilla top; nuclei not present. (High power.)

There do occur, however, as Olshausen points out, glandular cysts with true papillary growths; in these we can see in microscopic preparations cut obliquely, seemingly isolated, rounded or oval epithelial figures surrounding a stroma in their centers. If the section has been cut obliquely, it is necessary to identify true papillary growths by serial sections; these determine that papillary masses are found in the cavities and are not obliquely cut septa which passed through, and around which epithelial cells have grown (fig. 802). In the majority of cases there are no macroscopic vegetations and only seldom a cauliflower-like appearance. We can call these tumors, which v. Velits believes a subdivision of simple cysts, "papillary pseudomucinous cysts" (Pfannenstiel). They have the same tendency to be bilateral as the papillary ciliated epithelial cysts. Occasionally the papillary growths appear on the outer surface and may be implanted and give rise to peritoneal metastases which imitate the interior of the original cyst. Similar metastases arise from ciliated epithelial cysts (p. 882). Otherwise they behave exactly like the ordinary simple cyst, *i.e.*, make little trouble, do not cause ascites, are entirely benign, produce no distant metastases, and are easily differentiated from papillary ciliated epithelial cysts which are the most frequent of papillary ovarian cysts, but which have been poorly named "papillary cyst adenomas."

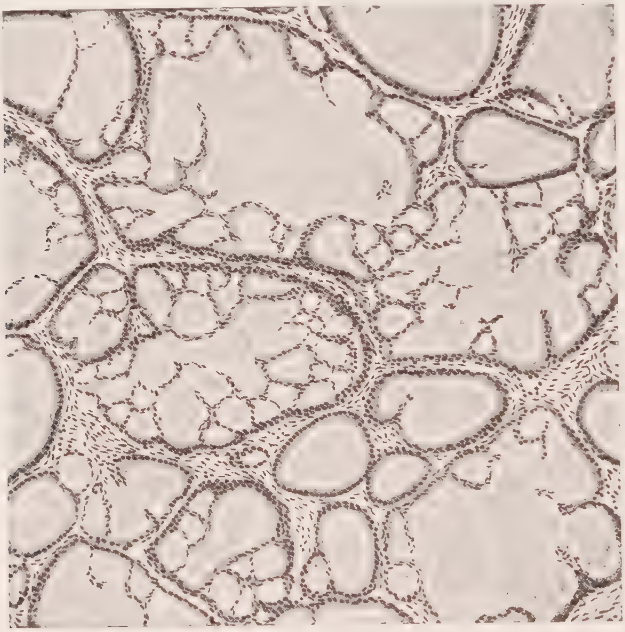


Fig. 803.—Pseudomucinous cystoma of ovary; from finely honey-combed more compact area of a cystoma; with otherwise large cystic spaces; tumor size of a child's head. (High power.)

Papilliferous or Papillary Cyst Adenomas (Ciliated Papillary Cysts). These tumors are usually of slow growth, of moderate size, and never reach the volume so common in glandular cysts (Olshausen). But they have been observed as large as a man's head. On the inner walls of the cavities, there grow true papillae, composed of richly vascular, often edematous at the tip, poorly cellular connective tissue stalks covered by ciliated epithelium (fig. 806). These grow into the cyst cavity and are of warty, shredded or dendritic appearance. Occasionally, the grayish red, soft papillary growths are very luxuriant (see fig. 805). The cavity, at first filled only with fluid, now is filled with many larger or smaller richly vascular red or white granular or cauliflower-like tumor masses (Fig. 804). The larger the cyst the more certain that most of the wall is smooth and only a small part is covered with papillae. (Olshausen.)

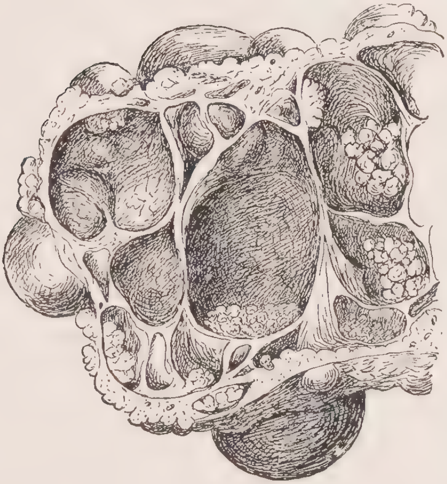


FIG. 804.—Piece of section of a papillary cystadenoma of ovary; (ciliated papillary cystoma) with papillary proliferations on surface, bilateral; woman 62 years old; ⅔ nat. size.

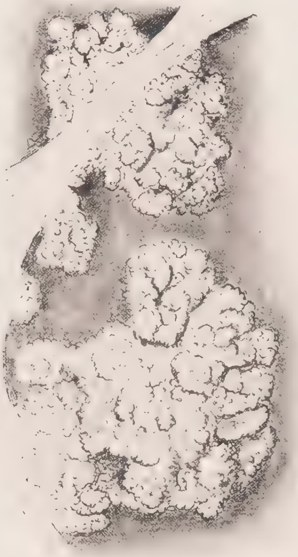


FIG. 805.—Piece from section through a polycystic papillary cystoma of ovary the size of a fist; proliferations very luxuriant; woman 34 years old; other ovary similar; ⅞ nat. size.

Thus, in a 37 year old woman, a unilocular cyst, twice as large as a man's head, was found to contain only clear serous fluid, and on its inner surface, papilla could not be seen; microscopically, however, small papillary cysts, with ciliated cells, could be found in various situations.

The papillary growths break through the wall of neighboring cysts or the main cyst, even though the main wall is, as a rule, much thicker and tougher than the wall of simple cyst adenomas. Cauliflower-like masses with thicker or thinner stalks are then freed in the abdominal cavity. At the same time, independent papillary growths appear on other parts of the surface. In three-fourths of the cases, the tumors are bilateral and in the great majority are extra-peritoneal, *i.e.*, between the leaves of the broad ligament (intra-ligamentary), and therefore covered by peritoneum. Their situation often induces pressure symptoms. The cyst contents are usually thin, and watery, or serous, at least never more than a trifle viscid from pseudomucin. Very frequently, calcified granules, the so-called psammoma bodies, are found in papillary cysts, while they are very uncommon in simple cyst adenomas. In places the papillae may feel sandy.

These psammoma bodies (corpora arenacea) are composed of calcium carbonate and an organic framework, built up concentrically; they look like mulberries, or have an uneven contour; they are found in the connective tissue of the cyst wall as well as in the papillae (see also under dura).

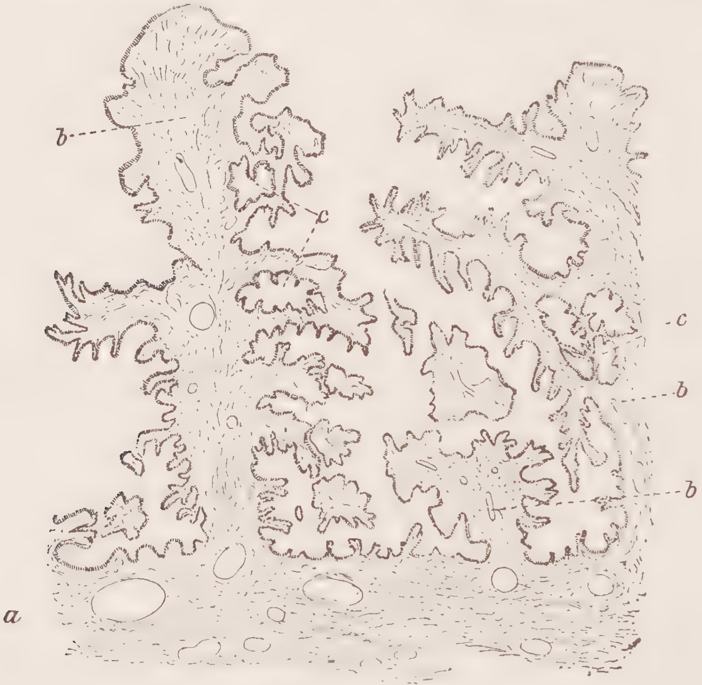


Fig. 806.—From a cystoma with several compartments; papilliferous cyst adenoma of ovary imbedded in celloidin. a, piece of septum; b, stroma of larger papillae with numerous branchings and covered with cylindrical epithelium; c, cross sections of epithelial depressions; here and there vessels in septum and papillary stroma; between the papillae some cross sections of papillae (apparently free). (Med. magn.)

The epithelium of the papillae is, in general, cylindrical, but as Olshausen and others point out, may vary and be in part ciliated and high, in part non-ciliated and lower; the nuclei are relatively much larger than those in cyst adenoma simplex and are more in the middle of the cells and not along the base as in the latter.

Just as in pointed condylomata (p. 1537), the growth of the papillae and other similar papillary epithelial growths is not stimulated by the connective tissue, but is started by the activity of the epithelium itself. The growing cells cannot stretch out in their width, but they force themselves upward and downward. They may grow upon each other, or they may pull with them, into the cyst cavity, some connective tissue which has blood vessels growing into it; adhesions may produce tubular lumena; or as they grow into the depth of the cyst wall, they drag the papillae in a way similar to that in the surface epithelial papillomas (Frommel). (See also p. 1569.) Metastases, or better, implantations, of tumor parts into the abdominal cavity, are frequent (p. 882). Ascites, often bloody, may follow. In diffuse growths, ascites is the rule.

Differentiation of Simple from Carcinomatous Papillary Cysts.—In macroscopic appearance, these multilocular cystic growths show many points of similarity, particularly in the build of the tag-like parts of the tumor. They both have the outspoken tendency to bilateral growth and to the development of psammoma bodies; the latter, however, are much more frequent and more numerous in papillary cyst carcinomas. The carcinomas are characterized, however, by their rapid growth, the development of true metastases through blood and lymph channels, as well as by the massive accompanying ascites. There are many solid medullary or softened white places on the section surface of a carcinomatous papillary cyst, in the septa as well as in the papillary parts, which even macroscopically can be seen to be built in alveolar form. Microscopically, in a carcinoma there can always be found here and there alongside of typical adenomatous places other than in the papillae, solid parts, in which there is typical adeno-carcinomatous architecture, which has, even though in miniature, papillary character; but there are also places in which solid carcinomatous nests can be found, as in solid carcinoma simplex or medullary carcinoma. In the papillae themselves in carcinoma, there is a polymorphy of the epithelium covering the papillae, there is irregularity in form, there are larger groups of epithelial cells and many layers just as in other papillary carcinomas, *e.g.*, in the bladder (p. 1433) or the uterus

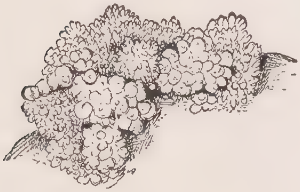


FIG. 807.—Papilliferous cyst-adenoma (psamosum) of ovary; piece from the surface; nat. size.

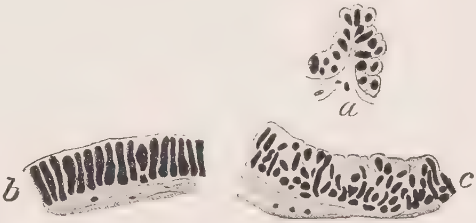


FIG. 808.—From a papillary cyst carcinoma; three separate parts with quite varying epithelium; a, cells small in several layers; b, large cylindrical with large nuclei; c, quite polymorphous, very irregular, several layers (high power).

(p. 1685). Pictures with such differing character as in fig. 808 *A*, *B*, and *C*, occur in one and the same section (we may well believe that such pictures come from a number of different tumors), and yet even these pictures do not give a correct idea of the variability of the tumors. Many layers of many kinds of cells, even resembling squamous epithelial cells, and many degrees of staining are undoubtedly a sign of carcinoma; on the other hand, many layers of fairly similar cells can be taken only as a sign of lawless epithelial production. Occasionally, a carcinomatous papillary cyst in the place of the papillae contains big glandular masses of many layers of epithelial cells breaking through into the connective tissue (see fig. 809). Martin who saw this form in a Fallopian tube, called it carcinoma gyriforme.

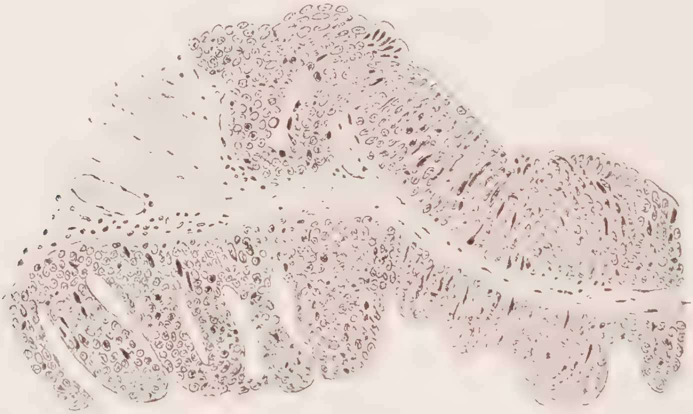


FIG. 809.—From a papillary ovarian carcinoma of a virgin 45 years old; thick glandular, fenestrated and convoluted polymorphocellular epithelial coating on a delicate fibrous core. (High power.)

Secondary Changes in Cyst Adenomas.—Fatty degeneration of epithelial cells and leucocytes can be observed in the cyst contents. In the yellow contents are also found fat droplets, fat granules, and cholesterin.

Hemorrhages are quite common (lit. O. Schaffer); hemorrhagic infarction occurs in torsion of the pedicle, see p. 1565.

Inflammation of the wall with exudation and pus formation, or suppuration and phlegmon may follow the direct transportation of pus or gangrene-producing bacteria through puncture, through the blood stream, *e.g.*, in typhoid fever, (see p. 796), sepsis, from an infected placental site, or through the lymph channels from an infected pelvic organ, or by continuity from a peritonitis, or through adhesions with the intestines, (see Mangold). Perforation may occur into the rectum or into other parts of the intestinal tract, or more rarely into the bladder, vagina, or through the skin. Rupture, as the author saw in a rare case, from ordinary pressure atrophy exerted by the cyst, perforated the bladder, rectum, sigmoid flexure and ileum. (Published by H. Martin.)

Calcification.—The psammoma bodies have been mentioned; further, calcification is seen in cells in the cyst wall, as well as between the tissues of the wall.

Spontaneous perforation without inflammation; if it occur into the abdominal cavity, there develop a diffuse pseudomyxoma, or an enclosed cyst or papillomas. (See under peritoneum, p. 882.)

Tuberculous infection has been observed in a few cases (see lit. by Schottlander, Wechsberg, Prusmann, Tusini, Garkisch, lit. Rosenthal, Cohn, lit. Stahr, lit. Moench, lit. Pribram).

Transformation into Malignant Tumors.—The stroma may at times become sarcomatous; in other cases the transformation is carcinomatous, in both simple and papillary cyst adenomas. Occasionally, only a small part of a large tumor becomes malignant and may be overlooked until later metastases are found in internal organs (lymph nodes, liver, bones, and so on). Compare the author's observation, p. 1573. There also occur carcino-sarcomas (Rothacker). Schultze-Heubach (lit) described metastases in the spleen of a pseudo-mucinous cyst which became a multicystic tumor, perhaps from implantation into the hilum.

Torsion of the pedicle and its consequences. When the growth of an ovarian cyst proceeds from the hilum of the ovary, it becomes intraligamentary, or grows free into the abdominal cavity with a pedicle from the ligamentum ovarii, the broad ligament, or occasionally from an hypertrophic tube. If, as is common, the tumor grows up from the pelvis, the pedicle torsion is spiral as follows: to the left it runs to the right, to the right the spiral runs to the left to 180 degrees, 360 degrees or more (Kustner). Others violate every rule (Goldberg). Torsion produces complete obstruction of the blood vessels with resultant total anemia and necrosis, or venous hemorrhages and hemorrhagic infarction. When pyogenic organisms are around, suppuration and softening ensue. Usually there are well defined peritoneal adhesions. Death occurs from autointoxication and nephritis (Brose).

Adhesions to neighboring parts, particularly to the parietal peritoneum and the omentum, are the rule in very large old tumors, *e.g.*, in the case illust. in fig. 799.

The Surface Papilloma.—It was stated above that growth of papillae through the wall of a papillary cyst adenoma out to the outer surface is common. In contradistinction, the tumor which has been poorly named "surface papilloma" of the ovary, has its primary papillary growth on the surface, usually in both ovaries, while the tumor itself grows freely into the abdominal cavity. There appears a large number of delicate, richly vascular papillae and aggregations of papillae looking like cauliflowers. They resemble quite closely the papillary tumors of the bladder. As the ovaries are covered with furry tags, they appear white or red and usually about the size of a child's fist. On section the ovary is sharply demarkated by its albuginea, and may be unchanged or perhaps smaller or slightly enlarged; not rarely it contains small cysts. Psammoma bodies are found also in these tumors.

Hofstatter doubts that there is such a thing as a primary surface papilloma, and believes, as does R. Meyer, that they are caused by the penetration of papillae from the inside of a papillary cyst.

These surface papillomata cause ascites and lead to implantation growths in the peritoneum (see p. 882). The histogenesis is discussed on p. 1569.

Histogenesis of the Simple and Papillary Cyst Adenomas of the Ovaries.—Many investigations have been made of the histological meaning of ovarian cysts, but it is only within recent years that satisfactory explanations of some of these structures have been forthcoming.

According to Klebs and Waldeyer, the glandular cystomas arise from Pfluger's tubes, those solid masses of cylindrical germinal epithelium, which, as we have assumed, are the embryonal forerunners of the Graafian follicles. (For newer views, see p. 1542.) The solid masses are said to give rise to cysts by secretion, analogous to the formation of the Graafian follicles; usually many cells are involved coincidently. If the epithelium of these cysts, *i.e.*, genetically, germinal epithelium, sinks into the surrounding connective tissue like tubes, and if these are separated from the main cyst cavity and stretched by secretion, new cysts arise; this process of epithelial displacement may keep up indefinitely. As the cysts grow, secretion from the lining cells and transudate from the blood vessels so stretch the walls that the latter disappear.

This conception has in time been modified in many directions. Since it is now assumed that the so-called Pfluger's tubes cannot grow in post-embryonal times (Waldeyer), they cannot, therefore, be the starting point of tumor formation in later years. Thus, the germinal epithelium, or, surface epithelium has come to be thought of as the place of origin of all new epithelial growths of the ovary (Hofstatter, Goodall). Isolation of the germinal (surface) epithelium into the stroma, and not of Pfluger's tube is, therefore, said to explain the genesis of simple cysts. While Waldeyer was demonstrating surface ovarian epithelium in relation to small cysts in older women, Nagel pointed out the frequency of epithelial inclusions and small cysts in ovaries showing chronic inflammation, and he was formerly of the opinion that all the epithelial tumors were related to these epithelial inclusions, the result of chronic inflammations. For the explanation of the genesis of ciliated epithelial cysts, much stress was laid upon the observation that the germinal epithelium (surface epithelium) may develop cilia under certain pathological conditions (Flaischlen). Moreover, a relationship between the tubule-like inclusions of surface epithelium in the stroma to ciliated epithelial cysts was found (Malassez, de Sinety, Flaischlen, Coblenz); then there was traced a direct connection between ciliated germinal epithelium and ciliated cyst epithelium, but, of course, only in the smaller cysts (Pfannenstiel). That findings in initial pictures are not entirely decisive in establishing the point of development of proliferating adenomatous tumors cannot, of course, be denied, but that the surface epithelium may at least be taken into consideration in the genesis of cysts, has been shown by Bauer in the institute of the author in Gottingen, by serial sections of one of the so-called struma ovarica cysts.

Furthermore, the possibility was mentioned that the granulosa cells of the Graafian follicles could be the point of origin of ciliated papillary cysts, as Marchand, v. Velits and others have assumed, but the granulosa cells as well as the ova in the primitive stage both arise from the germinal epithelium. In addition it may be mentioned that the germinal epithelium and the granulosa cells both have cilia in certain animals. In relation to observations such as those of v. Velits, which showed enlarged Graafian follicles, the epithelial granulosa cells of which had cilia and in which the disappearing ovum could still be found, we might think of the possibility of origin of ciliated epithelial cysts from the Graafian follicles. A number of authors finally assume that simple cyst adenomas also arise from Graafian follicles because of the finding of ova in young cysts (Steffeck), a view which seems to have some foundation; but, of course, these so-called ova were believed by others to be simply ovum-like cells undergoing vacuolar and other degenerations (Wendeler, Bandler). Pfannenstiel believes that the pseudomucinous cysts arise from follicle epithelium, but no one has as yet observed a transition of follicle epithelium into epithelial goblet cells as in glands. R. Meyer, Goodall and others oppose the view that cysts of any kind arise from Graafian follicles.

The older view that the ciliated papillary cysts, among other ovarian cysts, arose from rests of the primitive kidney, has again been revived (Nagel, v. Recklinghausen, Bandler, and others). In this connection the finding of epoophoron tubules in ovarian tissue is of importance (see the following chapter). But v. Franque, who observed one of the best cases in which there were primitive kidney rests particularly widely distributed in the ovary, is himself opposed to the possibility that cyst adenomatous tumors may arise from such structures. He believes that the only thing which occurs is a cystic dilatation, wherein the epithelium becomes flattened. For the new interpretation (Felix) of the earlier view that the prominent tubules of epoophoron or mesonephric origin were "rete ovarii," arising from germinal epithelium, and for differential histological points of both kinds of tubules, see p. 1569.

Congenital cell groups (squamous, ciliated, goblet) in the ovary and their relation to simple cysts and the proliferating adeno-cysts. While Waldeyer expressed the opinion that the goblet cells of the cyst adenomas arise from epithelial cell balls and tubules, differentiating from the very beginning into cysts and not into follicles. Burckhard first expressed the thought that in the further development of the tubules to a cyst there was also an anlage displacement of the connective tissue and the smooth musculature of the ovary; he actually showed in multilocular cysts a different stroma from that in the normal ovaries. This view has been confirmed by the examinations of Walthard, which were planned to show the origins of the proliferating ciliated and goblet cell adenomas. These results are more satisfying than those of former investigations and leave much less ground for former views, particularly those stating that inclusion of germinal epithelium is important in these cysts. Between the surface epithelium and the stroma, Walthard found small groups of cells which he regarded as predecessors of the surface epithelium, and which grow into tubules and become dilated into cysts, with pictures similar to those of small-cystic degeneration (see p. 1551). Furthermore, in the surface epithelium and in the stroma, he found groups of squamous epithelium from which small cysts were arising, (see p. 1554). And then it was possible to demonstrate islands of ciliated epithelial cells, both in the ovarian surface epithelium and in the stroma, without transition to surface epithelium; from both there arose independent tubules and ciliated epithelial cysts. Analogous groups of goblet cells were also found from which tubules and cysts arose. But it is particularly interesting that the stroma surrounding these ciliated or goblet cells and cysts varied in appearance. If the cells were present in typical ovarian stroma, they sooner or later showed degenerative changes. On the other hand, if the stroma, *i.e.*, the walls of the tubules, showed a different structure than the ovarian stroma (richer in cells), the conditions seemed to be present for a more pronounced growth. To sum up, there occur in the ovaries congenital masses of squamous, ciliated, and goblet epithelial cells which may be first, the starting point of temporary tubules and cysts, either in the interior of the ovary or in connection with the surface, or secondly, which may give rise to proliferating ciliated or goblet cell adenomas, *i.e.* cyst adenomas, in the latter of which the stroma around the tubules is demonstrably different from ovarian stroma and shows a distinct tendency to proliferation. (See also Lahm.)

The combination of dermoid with pseudomucinous and serous cysts is well known. For this reason a teratomatous origin of certain pseudomucinous cysts has been postulated (ovulogen, see Goodall and others); Hanau speaks of a unilateral entoderm-teratoma, and even R. Meyer believes the most likely origin of pseudomucinous cysts is teratoblastomatous.

The **surface papilloma** is supposed to arise from the surface epithelium, formerly called germinal epithelium (Frommel). Clefts, or berry-like, or glandular inclusions which later proliferate are said to grow into the stroma from cilia-bearing cells on the surface. Coblenz calls these inclusions "adeno-tubes." Papilla arise from them, gradually become vascularized and show as tags or arboreal growths from spaces on the surface. (Lit. by Williams.)

Appendix: Parovarian Cysts—or better—**Epoophoron Cysts.**—The epoophoron (Waldeyer), or the parovarium, is a body looking like a comb, inserted between the ovary and the tube near the fimbria and between the leaves of the broad ligament, *i.e.*, in the mesosalpinx (p. 1464). It is a remnant of the anterior (upper) part (the sexual part) of the mesonephron, *i.e.*, the Wolffian bodies. The homologue of the epoophoron in the male is the epididymis. Histologically, it is composed of small, blindly ending tubules lined partly by ciliated epithelium surrounded by a spindle cell tissue which, according to some, contains muscle fibers (see below). The epoophoron is in close anatomic relationship to the rete ovarii (p. 1462), also supposed to arise from the Wolffian bodies, but now believed to grow, like the medullary strands, from germinal epithelium (Felix). Tubules of the epoophoron are occasionally connected with the rete ovarii, (in the male they are always connected with the rete testis); the thick walled epoophoron (mesonephrogenous) tubules with their high epithelium then communicate with the narrow spaces of the rete which are lined by low epithelium with darkly stained nuclei; the branches of the rete in the ovarian hilum send prolongations into the ovarian substance. (Buhler speaks of "ground strands," v. Franque, Rielander, lit.) The embryonal medullary strands, topographically homologous to the straight tubules of the testes (see p. 1542), and in early developmental time peripheral to the cortical layers and toward the hilum, are connected with the rete ovarii; some of them give rise to follicles (follicle epithelium, homologues of the convoluted tubules of the testes), while others undergo degeneration; the first to degenerate are the glands which contain ova (oocytes). In adults, true epithelial medullary strands are no longer present; occasionally, however, remnants are found from which perhaps those small cysts and tubules arise which radiate from the rete peripherally into the ovary (see R. Meyer, Weishaupt, lit.).

The **paroophoron,** remnant of the posterior (caudal) part (the secretory part) of the primitive kidney (mesonephron, Wolffian body), is, (according to Switalski, Aschoff, R. Meyer), sharply outlined between the last branches of the spermatic artery before it enters the ovary somewhat internal to the free border of the broad ligament, and directly underneath the anterior peritoneal leaf (Rielander); (compare the position of the analogous paradidymis or Girald's organ of the male, p. 1461). It consists of remnants of glomeruli and groups of loosely wound, ofttimes parallel, narrow tubules; in contrast to the epoophoron it has no particular connective tissue wall. The epithelium is not ciliated, but is simple cubical or low cylindrical. Usually it contains a brown, noniron-containing pigment. According to Waldeyer, it disappears entirely before the end of the first year, according to Rielander, after the fifth year, and leaves no trace. But parts may remain, and later become the starting point of small cysts, and also, according to the disputed points above mentioned, to cysts of the ovary, or particularly to adenomyomas of the uterus and walls of the tube (see p. 1463 and under myomas of the uterus, p. 1659); but in the case of mesonephric tumors (Pick), there are pathological remnants of kidneys in addition to the paroophoron and epoophoron. (For further details, see Rielander, lit.)

Parovarian Cysts.—Cysts of various sizes may develop from the epoophoron. As a rule, they are unilocular with thin, relaxed walls; they contain clear, colorless, or opalescent fluid of low specific gravity, usually with no pseudomucin and very little albumen. They are lined by cylindrical or cuboidal, usually ciliated, epithelium. Their rate of growth in general is slow (Olshausen). The very small cysts are quite common; larger cysts are rare. The tumor as a rule is relaxed and fluctuating, lies between the leaves of the stretched broad ligament which may retain its structure more or less, is covered entirely by peritoneum which can usually be peeled off quite easily, and its vessels cross with those of the peritoneum.

Microscopically, the wall consists of two layers: the inner "membrana propria" is chiefly sclerotic connective tissue. Circumscribed thicker areas resemble papillae or warts on the inner surface. There is usually no smooth muscle. The outer wall is made up of tissue from the stretched broad ligament, its fibro-muscular parts more or less well preserved according to the size of the cyst. In small cysts, epoophoron tubules can still be demonstrated in this layer. Small cysts may even communicate with an epoophoron tubule (Schickele).

The general color in situ is, as a rule, darker than that of ovarian tumors and more greenish white; there are usually no adhesions. Large tumors are covered by the Fallopian tubes firmly adherent over their entire surfaces, while the fimbriated ends extend out over their posterior surfaces. (In the ordinary intraligamentary ovarian cysts, on the contrary, the tube is not fastened; since the tumor cannot involve the ligament up to the tube, they are separated by a portion of the mesosalpinx.) The tube is markedly stretched and flat, and with the exception of the fimbriated end, tightly adherent, but a probe can usually be passed through. The ovary also may be pulled out into a small flat body, lying mostly on the under surface without connection to the cyst wall. These thin-walled cysts have a tendency to rupture, but the results are generally not serious; frequent ruptures lead to adhesions with the peritoneal surfaces.

See Goldschmidt (lit.) concerning malignant tumors of parovarian cysts.

The rete ovarii (p. 1569) may also give rise to cysts (Ameschott) which Schickele calls "medullary" cysts of the ovary and which, of course, are of mesonephric origin; they may easily be mistaken for epoophoron cysts, since they grow within the ligament and involve the tube; there is always, however, a part of the cyst in the stretched out ovary.

The rare lymph cysts (cystic lymphangioma of the broad ligament) should give no differential diagnostic difficulties, (Lion, Schickele).

The rare adenomyomas of the epoophoron and the more common so-called paroophoron adenomyomas are discussed under adenomyomas of the uretus, p. 1661.

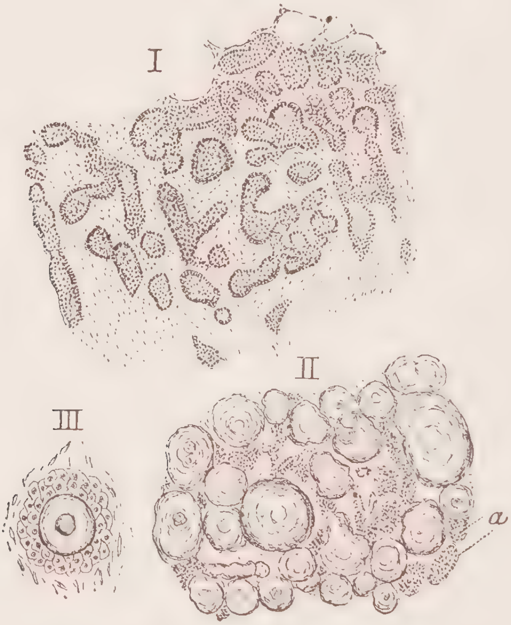
Malignant Epithelial Tumors.—**Carcinomas** are the most important of the malignant tumors. They are characterized histologically by an extraordinarily variable structure, especially those which arise in children. They are the most malignant of the carcinomas of the genital organs; the prognosis is very grave. They may occur before puberty, indeed even in small children; see lit. in appendix.

As points of origin, the germinal epithelium or the follicle epithelium is mentioned; in other cases, a previously benign tumor becomes a secondary malignant one. There may be differentiated: (*a*) solid carcinomas, (*b*) carcinomatous cysts. The former, less common, may infiltrate the ovary diffusely and enlarge the organ without, however, changing its form for a long time. Later it may reach the size of a man's head, and is then spherical with a nodular surface. The medullary carcinoma, the more common, has a soft marrow-like section surface, white or marbled. Scirrhous carcinomas are harder. Other forms show the structure of adenocarcinoma (fig. 809) with many variations, in which, even in solid appearing tumors, are cystic or cystic-adenomatous spaces as well as papillary growths. Spontaneous rupture has been observed.

All carcinomas of the ovaries tend to be bilateral. Heinrich assumed, probably incorrectly, (see Glockner), that the bilateral involvement is practically always a metastatic manifestation from one or the other side.

In adeno-carcinomas particularly, this is easily shown to be incorrect by the microscopic examination.

Regressive metamorphoses are common, such as hemorrhage, fatty degeneration, calcification, necrosis, softening of the cells, or of the stroma and subsequent liquefaction cysts. When there are adhesive inflammation and carcinomatosis of the peritoneum, and when the ovaries are only moderately enlarged, covered by adherent loops of bowel and fixed between the uterus and rectum in the true pelvis, the diagnosis of the point of origin of the adhesive peritoneal carcinomatosis may be very difficult, even at autopsy. If calcification occurs, an extraordinarily large number of irregular psammoma bodies are often found in the interstitial tissue and the carcinomatous tags; in the latter, the calcification occurs in the epithelial cell masses or in their hyalinized remains. The tumor tissue appears pale yellow white, granular and hard as mortar; on section it feels like rough sand paper; squeezing between the fingers liberates rough sandy bodies. At times, there is ossification (Buch). Ovum-like structures in ovarian carcinomas are well known to all experienced observers (see pages 1567 and 1553). The author saw them also in cyst-adenomas (Liepmann, Tusini, Schmincke, Blau, lit.).



Figs. 810–812.—Carcinoma of ovary. I. Adenocarcinoma with transition into solid carcinoma. II. From a solid psammo-carcinoma, predominant character of carcinoma simplex, the plain alveoli visible at a. The carcinoma nests are impregnated to a large extent by psammoma granules of rounded, pear-shaped and cylindrical forms. III. Psammoma bodies within a cancer nest (v. II). (I and II lower power; III medium magn.)

The carcinomatous cysts arise from transformation in a simple cyst adenoma or a papillary cyst adenoma, or they are malignant from the beginning, *i.e.*, true cystic carcinomas (Pfannenstiel). (See p. 1563 concerning papillary cystic carcinomas.) In both cases, there is a superficial resemblance to a benign cystic adenoma, and even histologically, a benign character may be present in spots. Not rarely, in very thick walls, *i.e.*, in quite old multilocular cysts with or without papillae, a few white marrow-like places show the histologic structure of carcinoma of the adeno type. In other cases, the carcinomatous foci are so small that it is only by finding metastases, particularly in the peritoneum and in the lymph nodes, that the malignant nature of a cyst is made manifest.

The development of colloid carcinoma in a cyst is rarer. At the autopsy of a sixty-two year old woman, the author saw a medullary carcinoma infiltrating through the capsule of a multilocular adeno-cyst; the walls were very thick and contained twenty-five liters of fluid; it arose in the right ovary. The carcinomatous places were very small; in other isolated places in the septa of the cyst there were macroscopic adeno-cystic structures. Many metastases had arisen from this tumor; the markedly thickened retroperitoneal lymph nodes were nodular, on section like swollen sago and grayish white; in the liver were carcinomatous nodules as large as a fist, hemorrhagic, in part, light colored and necrotic, and white in other places.

Granulosa Cell Tumors: Solid to Many Cystic Structures.—Recently, much attention has been paid to the folliculomas (lit. Aschner) or the granulosa cell tumors (v. Werdt), the latter name preferable, since it is also useful in solid tumors, or the carcinoma ovarii folliculoides s. cylindromatosum (R. Meyer). The older conception placed the responsibility of folliculomas on misplaced ovum anlage and thus described them as primitive ova and primary follicles but this theory has recently been disputed by Blau and Ingier. Newer investigations have shown that the responsibility of these tumors rests upon unused, remaining parts of the epithelium of the granulosa balls, *i.e.*, the unripe anlage of the parenchyma (see p. 1542), and not on ripe follicle epithelium, *i.e.*, on completed follicles. Growths from the earliest stages result in solid alveolar granulosa cell tumors of which v. Werdt has described a case, which agrees in all particulars with the case of the author as illust. in fig. 813; these types are rare. Finally indifferent granulosa cell masses of small diameter are observed rather commonly. The next stages mimic, as Aschner described, the picture of primitive ova, *i.e.*, of the parent cells of ova, of course, very much undifferentiated. Primitive ova or ova themselves naturally are never present. In the masses of cells are many small spaces containing secretion or hyalin degenerated cells around which there are other cells arranged radially in simple formation. When the spaces with their hyalin contents become larger and the surrounding cells spread out over a broader space, growing follicles are imitated, and connective tissue snared off from the surrounding tissue may develop a sort of theca. Following this, cystic transformation and enlargement may take place even to macroscopic cysts. But with all this, the large variety of types is still not explained (R. Meyer). According to Aschner (lit.), those tumors containing many cysts show a cortical and a medullary layer. Their consistency is tough and elastic, the parenchyma is yellow. The size varies from that of a walnut to that of a man's head. Aschner differentiates between benign and malignant "folliculomas." There are, however, no histological criteria; microscopically they all appear to be carcinomatous; metastases may be present or absent.

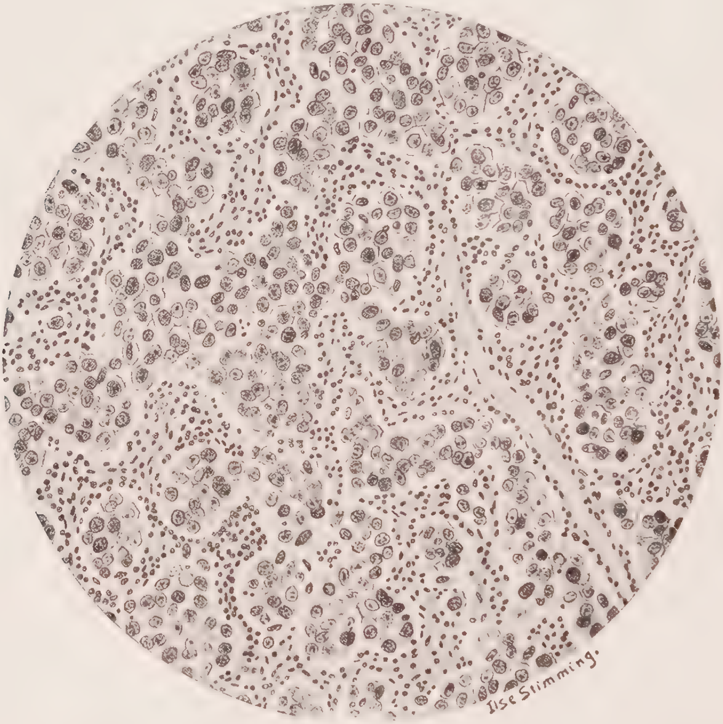


FIG. 813.—Solid carcinoma of the type of solid granulosa cell tumor of v. Werdt. Between the strands of polygonal cells with large nuclei, moderately vascular, fibrillary connective tissue infiltrated by lymphocytes. From a firm ovarian tumor from a girl 20 years old; tumor 14 × 9 × 6 cm. On cross section appearance uniform, cloudy hazy gray white to yellow; only isolated strands of connective tissue suggest divisions with their wavy lines, but few glassy transparent places here and there indication of a cortex with more dense fibrous arrangement. (Med. magn.)

Chenot calls attention to the similarity of certain ovarian tumors to the structure of "seminomas," (see p. 1501, the large cell testicular tumor), which can be seen by comparison with our case in figs. 775, 778 and 813; he believes they are due to the growth of indifferent cells of sexual-embryological derivation, snared off in the sex glands and differentiated into either the male or the female type.

R. Meyer (lit.) has written of particular forms of carcinomas in hermaphrodites and others with genital anomalies; the tumors are made up of large round cells closely packed, without interstitial substance, and with a great tendency to necrosis and hemorrhage. Others have called these tumors "alveolar sarcomas."

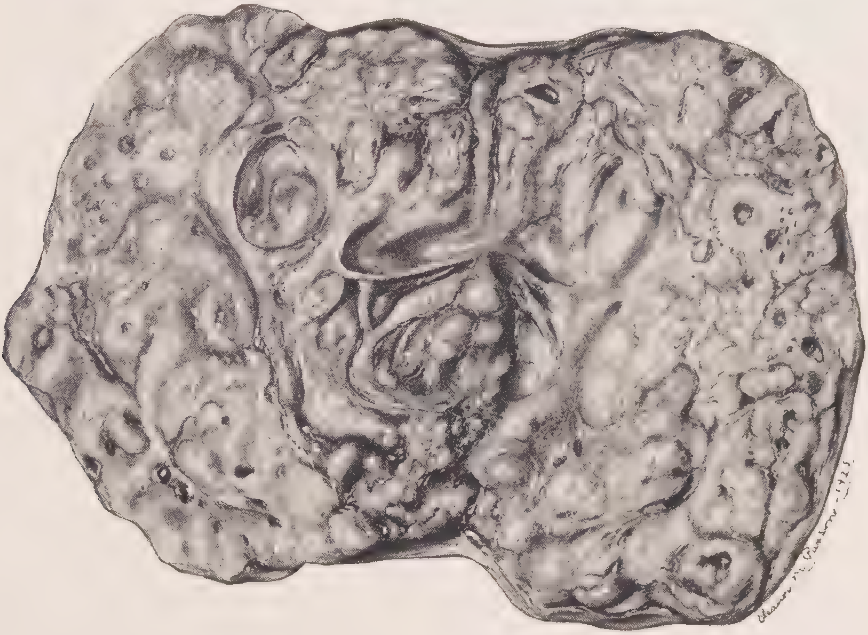


FIG. 814.—Corpus luteum adenoma of left ovary of child seven years old. This child began to have menstrual discharges about six months previous to operation. Showed growth of hair in axillae and on pubes and growth of figure to womanly proportions. A mass was found in the abdomen by the mother several weeks before operation. This was removed easily and proved to be a corpus luteum adenoma. The child immediately ceased menstruating and has grown to reassume its childish figure. (Two years post operative history.) L. H. #19339. ⅝ nat. size.

The literature concerning the rare hypernephromas of the ovaries, which may become as large as a man's head, can be found by Vonwiller and also p. 1290. See Peham.

A primary ovarian carcinoma may produce implantations on the uterus, tubes, and peritoneum, as well as hematogenous or lymphogenous metastases to these or other organs, but this complication is rather uncommon.

Secondary ovarian carcinomas appear by continuity or by way of the lymph route, *e.g.*, from a uterine carcinoma, particularly from the body of the uterus (lit. Schlagenhaufer, Glockner, Offergeld, Schottlander,

Schottlander-Hermauner; the lymphatic route is rare, see Frankl), or by way of the blood stream. They are diffusely infiltrating, solid or medullary, nodular, or even cystic (see Amann), and fairly common as the pathologist has long known, but the gynecologist has only recently come to realize. They are often bilateral and may reach the size of a child's or man's head. They are quite common in primary carcinoma of the gastro-intestinal tract, particularly of the stomach, especially the diffuse infiltrating forms; the author saw colloid cystic metastases arise from a very small microcystic gelatinous adeno-carcinoma in the gall bladder; metastases in the peritoneum and in the portal lymph nodes were also found, (see Omori, Gouilloud, Bland-Sutton, Brunner, lit., Kohlmann). In a fifty-two year old woman the author saw a bilateral ovarian carcinoma as large as a hen's egg coming from a carcinoma of the rectal wall which had continued into the peritoneum. They are also secondary to tubal carcinomas. Occasionally, secondary growths are found in the uterus from primary tumors in the stomach (Schenk and Sitzenfrey); according to Frankl these endolymphatic metastases are quite common in the mucosa or the muscularis of the uterus, or in the tube.

The routes taken by metastases to the ovaries may be summed up as follows:

1. The retrograde lymphatic route. Cells in the lymph channels reach the hilum of the ovary. Roemer, Glockner and others point out these paths, and experiments by Wolfheim have confirmed their views. Frankl believes the lymphatic route is the most frequent way of propagation. In a twenty-five year old woman with a carcinoma of the stomach, and in a fifty-four year old woman with carcinoma of the stomach and the peritoneum, the author saw retrograde transportation by way of the lymph channels even into the tube, and what is very rare, into the kidneys (see p. 1390). (The ovaries of the first named woman were exactly similar to those in fig. 815.) Similar metastases have occurred from breast carcinomas, where the lymph channels of the pleura, diaphragm, peritoneum and the larger lymphatic node systems transport the metastases.

2. Hematogenous metastases are frequent from breast carcinomas. The work of Hallauer has shown how little known this phenomenon is. In a forty year old woman, the author saw metastases in both ovaries and very numerous growths in the brain arising from a breast carcinoma. In a fifty-seven year old woman with osteoplastic carcinosis following cancer of the breast, both ovaries were little enlarged and were freely movable, but thickly infiltrated with carcinoma, while the peritoneum was entirely free. The author even saw hematogenous metastases in the ovaries from a carcinoma of the thyroid gland, an event which is quite

uncommon. Chiari, as well as Ribbert (lit.), describe similar hematogenous metastases; as a rule, however, secondary ovarian carcinomas develop from breast tumors by way of the lymph channels as the author has demonstrated in very many cases. (See also Bland-Sutton.)

3. Metastatic ovarian carcinoma frequently begins on the surface or in the cortex as nodules or as a thick coating covering the outside. More rarely, distinct nodules grow in the interior of the ovary. Later there develops a homogeneous infiltration. Kraus, Schlagenhaufer, Polano, Frankl and others, believe the most frequent mode of metastasis into the ovary from a primary carcinoma in another abdominal organ is through implantation of the cells on the surface and then infiltration into the tissues, particularly through the lymph channels. This presupposes that there are carcinoma cells free in the abdominal cavity, and since superficial nodules in the serosa are frequent, this is not difficult to assume; furthermore, this view assumes that the cells are able to infiltrate into the surface of the ovary just as wandering cells loaded with India ink in a rabbit are able to do. It is also necessary, as Wolfheim (Schottlander) points out, that the surface epithelium of the ovary be injured, a circumstance which occurs at every ovulation (rupture of a follicle). Sitzenfrey, however, found implanted carcinoma cells between the germinal epithelial

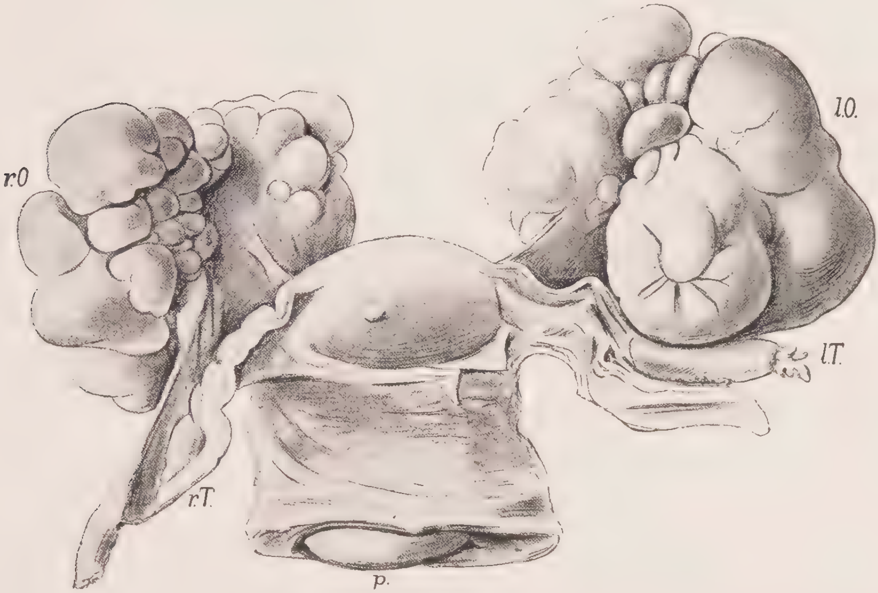


FIG. 815.—Bilateral metastatic carcinoma of ovaries (adenocarcinoma) from carcinoma of stomach (adenocarcinoma). r. o, l. o,—r. and l. ovary rT, lT,—r. and l. tube; p, os uteri. The markedly anteflexed uterus shows a small subserous myoma; woman 70 years old; ¾ nat. size.

cells, and Kohlmann points out that the closely packed germinal epithelium is not able to withstand the entrance of carcinoma cells and they may be implanted without previous lesion. Of course, the predilection of the cortex of the ovary is easily understood if the implantation mode is frequent. (This is analogous to implantation in Douglas's cul de sac; see Rosenstirn.)

Ovaries as large as a child's head, or larger, have often been seen. Thus the ovaries of a forty-one year old woman with a carcinoma in the middle portion of the stomach reached the weight of sixteen pounds. The right ovary was adherent in the true pelvis and compressed the right ureter; the other lay in the hollow of the sacrum. In another very instructive case, the ovaries reached almost the same size. (Forty year old woman, pyloric carcinoma; gastroduodenostomy performed three years before, diffuse carcinomatous infiltration of the peritoneum and the pleura, nodules in the liver and pancreas.) Usually, however, the enlargement is of less degree. Occasionally, particularly in primary carcinoma of the stomach, microscopic carcinoma may be found in ovaries which appear normal macroscopically.

The ovarian stroma reacts to the infiltration of metastatic cells in various ways, sometimes with a richly cellular sarcoma-like proliferation, or more frequently, with a very marked connective tissue growth. Growth of the epithelial elements may then be hindered. Metastatic scirrhous carcinoma may easily be confused microscopically with sarcoma and thus be mistaken for a primary ovarian tumor (see under fibromas); it has even been thought, but erroneously, that such persons have a particular predisposition to the development of many primary tumors (Rubeska, Pfannenstiel, Engelhorn); Schlagenhaufer (lit.), Roemer and Glockner, as well as others, have shown the true state of affairs in a way which agrees with our experiences.

F. Krukenberg has described as "fibrosarcoma ovarii mucocellulare carcinomatodes," (a rather poor designation), diffusely infiltrating, bilateral ovarian tumors consisting of larger swollen signet ring cells along with other epithelial cells, which spread out between a richly cellular connective tissue. That such tumors really do occur as primary growths, (see also Glockner and Schenk), is doubtless true, (see Frankl, Marchand), but they are rare. Wagner was no doubt correct, when he pointed out that most of the cases are in reality metastases of a scirrhous gastric or intestinal carcinoma, which show mucoid changes either in the primary tumor or perhaps first in the metastases; through lymph stasis and its subsequent edematous saturation, the vigorously growing connective tissue resembles a fibroma or a fibrosarcoma, particularly because it involves, as a rule, the interior of the tumor which is often surrounded by a tough cortex of connective tissue as thick as a finger. At the examination of such "Krukenberger's tumors," the author has frequently predicted that an occult primary carcinoma of the stomach would be found, and often this opinion has been confirmed at autopsy. (See also Stickel, Sandrock, Cohn, Ulesko-Stroganoff, Hussy, Paul Hartmann and Metzger lit., van der Perk.) The same skepticism should be exercised in relation to many tumors which have been described as endotheliomas of the ovaries (see p. 1581; Polano and Pepaioannou).

Benign and Malignant Connective Tissue Tumors.—Enchondromas and angiomas (lit. Kroemer) are very rare. Fibromas, which may occur

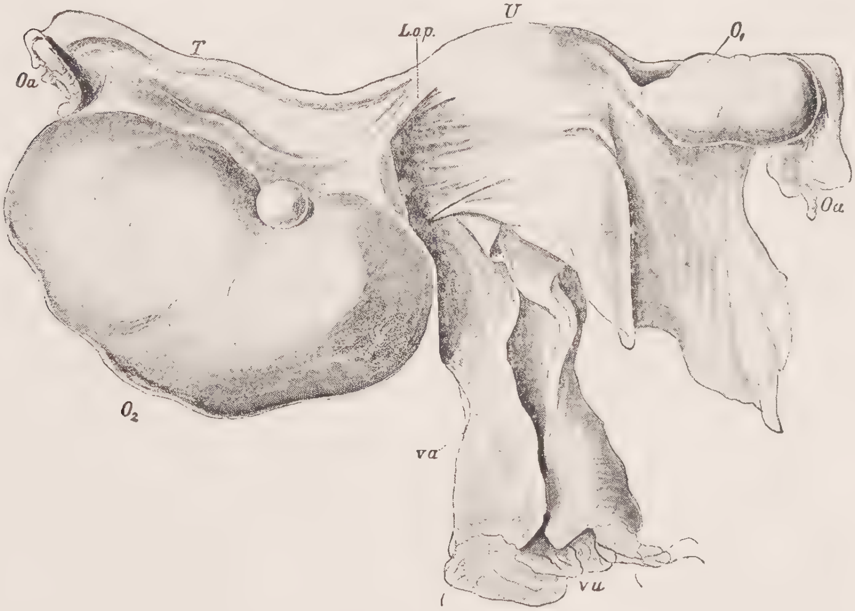


FIG. 816.—Spindle cell sarcoma of both ovaries, posterior view. The l. ovary (O2) on which another small globular tumor is growing is much more enlarged. T, tube; Oa, distal end of tube; Lop, ovarian ligament stretched out; U, uterus covered with peritoneum; va, vagina; vu, vulva; ½ nat. size.

at any age, are seldom large. The smaller examples are occasionally flat or lobulated papillary growths on the surface of the ovary; larger examples are tuberous, flat, whorled, solid, perhaps pedunculated; still others infiltrate the ovary diffusely; involvement is often bilateral; edema may occasion a myxomatous consistency. The ovary may become as large as a fist or larger; thus, in a seventy year old woman, the author saw an edematous fibroma as large as a child's head and weighing 1290 grams; in a seventy-three year old woman, he saw a fibroma weighing 4320 grams, and with its pedicle twisted. The general contour of the ovary is usually preserved in the larger fibromas, as in fig. 816. Partial calcification is quite common, total calcification is rare. Torsion of the pedicle is relatively frequent (Mauthner, lit.). (Fibroma-adenocysticum, see Fleischmann, Mauthner, lit.) A metastatic tumor from a primary stomach or intestinal carcinoma may be hidden in a seemingly pure fibroma (see Amann). Fibromyomas are quite similar; they are often difficult to distinguish from spindle cell sarcomas, (for the histology and differential diagnostic points, see under uterus, p. 1666); they are quite frequently bilateral. Total calcification of a fibromyoma is quite rare. Liquefaction spreads centrifugally from the center, and occasionally transforms the whole myoma into a cyst, just as in the occasional intraligamentary cystic uterine myomas. Ossification may also occur.

Primary sarcomas are relatively uncommon, are frequently bilateral and vary greatly in structure.

In 160 sarcomas found at autopsy in The Pathological Institute at Basle, (1.26% of all autopsies), twelve were primary ovarian sarcomas, which equals 7.5% of all sarcomas; in 1078 carcinomas (8.47% of all autopsies) 40 were primary ovarian carcinomas, *i.e.*, 3.71% of all carcinomas. The ages were as follows: 16, 25, 27, 28, 31, 32, 46, 47, 50, 54, 61 years. In twelve cases at Göttingen (operative material), the ages were 7, 10, 17, 19, 23, 45, 47, 50, 52, 58, 60, 63 years. Most sarcomas are composed of small or large spindle cells (fibrosarcomas are relatively benign), and the external surfaces are similar to those of fibromyomas and fibromas. The forms are usually nodular or egg-shaped; the section surface is fibrillar or fascicular. Myxosarcomas also occur. Many sarcomas are softer and are mixed with round cells; others contain polymorphous cells with many giant cells. Pure soft, round cell sarcomas are rapidly growing, are rare and very malignant; recently the author saw two in children of seven and ten years respectively; both tumors showed very marked fatty degeneration and necrosis.

Alveolar sarcomas are usually composed of large round cells similar to epithelial cells (Wolff, lit.). It is necessary to use great care in differentiating these tumors from carcinoma. In a fifty-eight year old woman, the author saw a fascicular spindle cell sarcoma of the ovaries together with an adeno-carcinoma of the neck of the uterus.

Isolated examples of primary melano-sarcomas occur in the literature: the case of Bab (lit.) is doubtful, not only to the author, but also to Kroemer; see the cases of Winternitz (lit.), Markus, E. Vogt, Herzog. Nowak disputes the occurrence of primary melano-sarcomas of the ovaries.

Irregular bulgings are very frequent in ovarian sarcomas, following myxomatous softening, hemorrhage, fatty degeneration, or necrosis in the tumor. There also occur degenerative cysts with smooth walls, and these may be mistaken grossly for true cysts. Occasionally, true cysts are found lined by epithelium. Sarcomas of the ovary occur mostly in early adult life, but have also been observed in children.

Sarcomas may be adherent to neighboring organs, and are often accompanied by ascites (according to the compilation of Zangemeister, 29 times in 36 cases). In a thirty-one year old woman, the author saw bilateral polymorphous and giant cell ovarian sarcomas larger than a man's head. There was an encapsulated pseudocystic collection of ascitic fluid in the peritoneal cavity, surrounded by a thick sarcomatous wall, the posterior surface of which was behind the coils of small intestines, and appeared as though covered by an icing of tumor tissue; below, the sigmoid flexure closed the space from the pelvis in which the sarcomatous ovaries were situated; toward the upper end, the sac reached to the liver which was pushed forward. The free peritoneal cavity covered the sac above and behind like a flat cap; the stomach was behind the sac. Occasionally pressure on the bladder and the rectum is very troublesome.

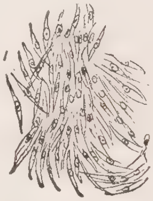


FIG. 817.—Spindle cells from a sarcoma of ovary (med. magn.).

Many sarcomas are complicated in their structure. Thus they may arise from the very smallest blood vessels (hemangio-sarcomas), in part as the so-called peritheliomas, or better, perivascular sarcomas arising from the cell bordering the adventitia (see R. Krukenberg, Apelt, Graefe, Barrett, lit., Goth), and in part as hemangio-endotheliomas (see fig. 231). In diagnosing the former, it must be remembered that many sarcomas have a perivascular structure without necessarily having any genetic relationship to the vessels (Ribbert). Other endotheliomas arise from the endothelial cells of the lymph spaces and from the flat cells of the stroma, in which case, the proliferating flat cells are cubical or cylindrical, and irregularly fill preformed spaces. Hemangio-endotheliomas are therefore differentiated from lymphangio-endotheliomas, as well as endothelioma "intravasculare" from "lymphangiomatosum" (Eckardt, Heinricius, Espelet, Kworostansky, Kubo, Kroemer, lit. in appendix); cylindromatous peritheliomas have also been considered as a particular form of the endothelioma (Zinsser, lit.). Other authors, as for example R. Meyer, Mauthner, are skeptical concerning the endotheliomas (see also p. 1579). Before the differentiation of endothelial sarcomatous tumors is made with certainty, it is necessary to be well acquainted with the varying types of ovarian carcinomas, particularly those which occur in younger individuals. There are forms with cells like granulosa cells, or with large nuclei, and which are subject to all sorts of degenerative changes (vacuolization, signet ring form, hyalin droplet degeneration); thus the epithelial complexes are more and more obscured, and remain as such only in small strands or spaces or tubules, lined in part with these flattened epithelial cells which may be mistaken for endothelial cells, or they are changed into a system of branching vacuolated cells; moreover, they may even lie in the neighborhood of blood vessels, and, when in masses, may very readily be mistaken for a perivascular sarcoma or a perithelioma.

The endotheliomas which are typical malignant tumors, are occasionally bilateral; they are mostly solid, nodular, tough or of medullary consistency; occasionally they are cystic in part or over larger areas (Burckhard); their structure is generally alveolar, and the reticulum is partly or wholly myxomatous with degenerative false cysts. If a true cystic character is manifested, they are spoken of as "endothelioma lymphaticum cysticum" (Schurmann, lit.).

According to Klemperer, the so-called endo- and peritheliomatous interstitial cell sarcomas of alveolar structure arise from the interstitial cells, *i.e.*, the analogues of the internal theca cells. They usually are solid tumors of considerable size (3 to 5 kilos), and found for the most part in younger individuals. Their similarity to the granulosa cell tumors cannot be denied, but v. Werth believes, probably correctly, in the epithelial nature of granulosa cell tumors. Goodall also, who believes that the peritheliomas of the ovaries are eight times more frequent than sarcomas and gives them microscopically a middle place between carcinomas and sarcomas, maintains that they arise from the interstitial cells which morphologically appear between the epithelial and the connective tissue cells. v. Werdt believes that many tumors reported as endotheliomas are in reality granulosa cell tumors (for instance the case of Kubo). Other sarcomas are occasionally combined with carcinomas (sarco-carcinomas). At another time they are combined with adenomas, particularly with cyst adenomas; the interstitial tissue is therefore sarcomatous (cystadenoma sarcomatosum). Even cylindromatous tumors have been observed, and others similar to the structure of embryonal adenosarcomas (see under kidneys, p. 1392, Glockner, lit.). Literature of sarcoma by Kroemer; of sarco-carcinoma by Rothacker, and Harbitz.

Metastatic ovarian sarcomas are rare; they are occasionally met in primary uterine or breast sarcomas (Segoud and Renaud), and are particularly frequent in melano-sarcomatosis as isolated multiple nodes, or as a diffuse invasion by a homogeneous tumor, or, as the author has seen, as cysts of considerable size marbled with black brown tumor masses like a tapestry, (see also E. Vogt).

Dermoid Cysts and Solid Teratomas of the Ovaries.—Dermoid cysts and teratomas are particularly hard to differentiate when they occur in the ovaries. Many, like Bandler, call them both dermoids, and distinguish between solid and cystic structures. Dermoid cysts in general are usually divided into (1) simple dermoids which are subdivided into (*a*) epidermoidal, *i.e.*, made up only of the epidermoid parts of the skin—these are rare in the ovary (Chapuis, lit.)—and (*b*) true dermoids which contain all the structures of the outer skin, glands, hair and a tough wall; (2) the complex dermoid cysts or cystic teratomas; (*a*) those of the ovary are always much more complicated. (The simple true dermoid cysts arising from ectodermal tissue misplaced in the course of development are as a rule different both genetically and morphologically from the dermoid cysts of the ovaries.) According to Wilms, we speak of dermoid cysts—cystic teratomas—embryomas—rudimentary parasites, when the structure is made up of fully differentiated tissues, organs and at the same time the rudiments of a fetus; solid teratomas—embryoid tumors, when the embryonal tissue retains its fetal character, *i.e.*, after reaching a certain degree of differentiation, it grows further in a lawless manner, without boundary and without giving rise to completed organs. The terms teratoma (our *a*) and teratoid (our *b*) are also used, the former describing a tumor made up of mature tissues put together somewhat like a human torso, the latter describing a true tumor (see Neuhauser) or a teratoblastoma (R. Meyer) (see also under testes, p. 1503). On the other hand, Askanazy classifies dermoid cysts and teratomas like the author; the former are composed in largest part, if not exclusively (see Kroemer lit.), of mature tissue; the latter are true tumors entirely or almost entirely made up of fetal immature tissues. The infrequent occurrence of such formations in dermoids or dermoid cysts can be explained by growth hindrances or atrophy of single parts. Differentiation reaches a much higher degree in the dermoids than in true teratomas (see Landau). There are also classified teratomas—tridermomas with mature, and teratoblastomas—tridermomas with immature tissues. Askanazy classifies according to the degree of maturity: coetane or adult, made entirely or almost entirely of tissues equal in age to those of the individual carrying the tumor; and embryonal teratomas made almost entirely of embryonal tissue parts. Nevertheless, there do occur teratomas which are closely related to dermoids (Sjovall), and Schwalb would like to discard the sharp division between the two.

Cystic teratomas—dermoid cysts (*a*) are congenital and give the impression more of cystic malformations than of actual tumors. The cyst is filled with fatty material which quickly solidifies when removed from the body, and large masses of blond or black hair; the inner lining usually shows in one place a very variably formed mass or protuberance, (the so-called anlage of the head, Wilms, see p. 1504). This is formed from ovarian tissue, the surface of which in the neighborhood is covered by squamous epithelium, and which contains, as a rule, many sweat and sebaceous glands (Klaussner). In the inner wall are variable tissues such as fatty connective tissue, muscle, cartilage, bone, (see Heijl), myxomatous as well as glandular structures of very varying forms; the latter are sebaceous, mucus, and salivary glands, some stomach and intestinal glands, etc; or the structures show simple or papillary masses covered by ciliated epithelium and thus are quite similar to some ovarian cysts. Teeth are quite common, sometimes in great numbers (hundreds), and not uncommonly there are also maxilla-like masses of bone, especially in the anlage of the head; they may be completely buried in this head anlage or may stand out as crowns in the inside of the cysts. The teeth closely represent the type of normal teeth (Moser); Bluntschli saw teeth from the second dentition. Finally the pieces of bone, which may jut out prominently on the surface of the tumor, show the most variable irregular forms. In occasional cases, usually in unilocular cysts, the ordinary hair and sebaceous material does not appear homogeneously mixed, but through the saponification of a part of the fat and mechanical disturbances in the fluidity of the suspended fat masses (Plenz), there appear many dermoid or fat marbles as large as peas or hen's eggs (lit. E. Schwalbe, Lippert, Guendet, Schroder, lit.). The wall may contain cystic spaces from dilation of the lymph vessels, (Pfannenstiel-Kroemer). Schottlander believes that the actual space in the cyst may possibly be only an ectatic lymph space, and Maresch showed that this space is similar to lymph vessels in which the dermoid fat is squeezed out.

Concerning malignant carcinomatous and rare sarcomatous changes in dermoid cysts, see H. Ludwig (lit.), Kroemer (lit.), Sievers (lit.), Williamson and Barris, Frankl. The carcinoma arises in the structure of the dermoid or it enters the structure from an ovarian rest (Eisenstadter). Kriwsky has described suppuration in a dermoid in typhoid fever.

Ordinarily there occurs but one large cyst; in rarer cases there are many in the same ovary or in both (lit. Novak, Kroemer). Their size varies from that of a pea to that of a man's head. They may at times reach even colossal size; thus in a thirty-five year old woman the author saw a dermoid cyst weighing eighteen kilos; it contained twelve liters of cloudy, bloody, mucoid fluid. They occur in children, but grow rather slowly, until puberty, when they may grow much more vigorously, and at that time may appear clinically as full grown cysts. Often, however, they remain stationary. They are prone to torsion and to adhesions to the neighborhood; suppuration is not rare, whereupon perforation into neighboring organs such as the bladder and rectum may occur; phlegmons have arisen in these structures. An hereditary tendency to dermoid cysts has often been observed (Koltinski, lit.).

Solid teratomas or embryoid tumors or teratoids or teratoblastomas give the impression of solid mixed tumors even though a large number of small and smaller cysts can be found; in them we see a heterogeneous mixture of immature tissues of the embryonal type coming from all three germinal layers. There are no fully developed organ parts; everything is mixed up helter-skelter. Solid teratomas are found much more frequently than cystic tumors in the testes (p. 1504); the reverse is true of the ovaries, but the solid teratomas found in the latter are larger and may reach the size of a man's head, even as large as 10 kilos (Horrmann). They are usually noted first after the age of puberty; most of them grow rapidly and without boundaries. Clinically they are almost all malignant (Sjovall), even though, as against the statement of Kroemer, they are anatomically speaking, not malignant (Franco), *i.e.*, there are cases which metastasize because the teratoma becomes in part carcinomatous or sarcomatous, and there are also cases in which the teratomatous tissue appears in the metastases, but in these, as in the main tumor, only the immature tissue is shown, or the embryonal tissue with a tendency to become mature. In these cases we are on the border line between malformations and tumors (see Heijl). In the metastases there are often not all of the components of the primary teratoma (see Sjovall). In the latter we cannot see malignancy from the tumor tissue itself, but if there are richly cellular mesenchymatous parts present, it is easy to be mistaken, and sarcoma or sarcomatous change in a teratoma may be diagnosed; Kroemer, however, goes too far when he denies even the possibility of such a change (see the case of Wernitz and compare Sjovall). The solid teratomata have tendency to local recurrence.

The Histology, and Remarks on the Histogenesis.—The much scattered tissues in dermoid cysts offer material for study and contemplation. In addition to those mentioned above, there also occur: thyroid gland tissue which may reach a high state of development and take on the character of a goiter, even a cystic goiter; struma ovarica is not always easy to differentiate from a pesudo-mucinous cyst, is almost entirely free of iodine and in hemalumeosin preparations and in other simple stains they may be exactly similar to cyst adenomas, (Bauer in the institute of the author); in other cases particular and special stains (see E. J. Kraus, cited on p. 505) show actual identity with thyroid tissue (Kafka, lit.), see lit. in appendix. There are further found: breast tissue, trachea-like structures (Baumgarten, Neumann, Saxer), medullated nerves and ganglion cells (Neumann, Marchand, Lazarus, Wolff), masses of glia, eyeballs, retinal pigment and plexus-like structures. Heijl believes that central nervous substance plays a dominant role in solid teratomas as well as in the structures resembling chorionepitheliomas which occur in testicular teratomas; see p. 1509.

Internal genital organs never occur in the teratomas of the ovaries, nor do liver and pancreatic tissues. This non-occurrence is quite important, as R. Meyer points out, *i.e.*, teratomas never have sexual cells in their substance, but are made up of purely somatic tissue. The teratomas can therefore not have arisen from cells with totipotential possibilities.

Wilms has given as his opinion that all teratomas of the ovaries (and the testes) arise from the three germinal layers, which in the ovary he believes to be from an ovum and in the testes from a male sex cell, both of which grow into tumors by reason of a sort of parthenogenesis. In their further growth, separate tissues are then differentiated, but are soon hindered in their development and are destroyed, while others, particularly the so-called head anlage, (see p. 1504 under testes), are allowed to grow further. This holds for the dermoid cyst; in contradistinction, the embryonal tissue in solid teratomas, after differentiation, is allowed to grow lawlessly and without boundaries. Others, such as Pfannenstiel and Kroemer, Arnsperger, have followed this idea of Wilms. But vigorous opposition was brought to bear by various authors such as Bonnet, Neck and Nauwerck, Saxer, Nauwerck, etc., because in mammals, such a parthenogenesis has been shown to be untenable (Bonnet). Wilms himself later replaced this theory of parthenogenesis with one concerning a genesis from isolated misplaced blastomeres which belong to the body of the embryo, but which are not attached to it (Marchand, Bonnet). Blastomeres are the first cleavage product of the impregnated ovum before the blastula stage; in the lower animals it is known that these structures, when isolated, can give rise to rudimentary embryos. For the blastomere theory, see the discussion by R. Meyer, even though not every one agrees with him when he states that the characteristic of dermoids of both the female and male genital glands, as well as occasionally of those in other situations, is the finding of derivatives of all three germinal layers, and even though they are not found in the majority of cases (p. 1504).

It is possible to postulate that a part, *i.e.*, an isolated blastomere (see also Geller), of the impregnated ovum from which the individual develops who carries the embryoma, is separated and misplaced from the neighborhood of the impregnated ovum at a very early time. The misplacement, however, may be looked upon as occurring in another way, viz., that for some reason the division of a blastomere was hindered, and that it was enclosed in the further differentiating germinal layers of the other blastomeres (see also Sieber); this snared-off portion, though hindered in its further growth, still has the potentiality of forming tissues from all three germinal layers, even though it form but a rudimentary embryo which would be a sort of brother to the carrier of the teratoma, or perhaps only certain organs or parts of organs. The ovulation hyperemia at the beginning of puberty might be an auspicious stimulus to growth, even though this blastomere cannot reach the size of the greater mass of the impregnated ovum. It does not seem, therefore, an important matter whether representatives of all three germinal layers can be demonstrated or not in the tissue product which has come from the secondarily misplaced germinal cells, because at one time, one or another of the tissues may have been hindered in their growth. There are, nevertheless, cases such as that of Saxer in which only a single tooth developed in the ovary from all three germinal layers; this was an embryoma but one which had developed unilaterally (Wilms, see p. 1504). Jung has described a pure enchondroma. Isolated cholesteatomas are unilateral occurring embryomas (Piltz). This is also true of the struma ovarica (p. 1585). Furthermore, it may be that the so-called inclusion is not of a totipotential germinal layer, (see Borst), so that, *e.g.*, it contains only ectoderm and mesoderm (cystoma dermoides biphyllicum, Askanazy, the so-called bidermoma), as in the cases of Nauwerck and others (lit. by Pick); or as in other cases, the tissue is able to give rise to only entodermal organs (gastrointestinal tubes) (Arnsperger, Katsurada).

The greatest difficulties in explanation are occasioned by the fact that the cystic and solid tumors have an almost unexceptional predilection for the sex glands. Wilms has tried to find developmental disturbances in the primitive tissue of the urogenital system, and assumed that fragments of germinal tissues might be hindered in their differentiation and become misplaced in the primitive kidney tissue. Bandler explained the embryomas by assuming that there was germinal misplacement in early embryonal life, whereby different cells of the mesoderm and the ectoderm coming from the Wolffian bodies and passages were carried over into the ovary. Bonnet, however, disputed the origin of these structures from embryonal misplacement (see also Redlich, lit.). R. Meyer tried to find an explanation in the topography of embryonal affairs, but his attempt is not entirely satisfactory. L. Loeb then emphasized the parthenogenetic idea; he found, at least in the ovaries of guinea pigs in 10% of the cases, structures which he regards as parthenogenetically growing embryomas without impregnation having taken place; in later studies such embryomas showed similarities to chorionepitheliomas. These observations to him mean that both chorionepitheliomas and teratomas of the ovaries do not arise from misplaced blastomeres, but occur because of "parthenogenetic impregnation." The hypothesis of Novak occupies a middle position; he believes that only the sexual blastomeres, in contradistinction to the somatic, a distinction which of course is not held important by many, (for instance O. Hertwig), are the points of origin of dermoid cysts and teratomas (see alos Prym). These segmentation cells are in a position to enclose parthenogenetic masses which are similar to rudimentary fetuses. Since these rudimentary fetuses arise from primitive sex cells, it is much easier to understand their frequent presence in the sex glands, a point which is not explained by the blastomere theory. Even at that, R. Meyer opposed this theory because he said it contradicts itself. With this in mind, it might be better to revive the hypothesis of Ingier (lit.), which in part is derived from the older conception of Fischels. According to this, the development of teratomas of the testes and ovaries occurs from germinal cells, (perhaps from misplaced germinal epithelium itself) which, unlike the other "somatic" cells which form the rest of the body, do not develop along the normal "pathway," but as "abnormal" derivatives of the germinal plasma. Teratomas therefore would arise from a pathological and not a parthenogenetic differentiation of germinal cells. Ingier assumed that the division of the segmentation cells along the developmental path is hindered by some cause or another, and while they still possess somatic potentialities, in their differentiation into pure sex cells and somatic cells, some of the latter are isolated in between the sex cells, so that finally they come to rest between and inside of the finished sex gland. Fischel sees an explanation for the more recently studied teratomas in the wide distribution of the primitive germinal cells in early times; these cells, in order that they may be concentrated, must wander over a large space, so that the opportunity is easily given for them to remain in an abnormal place outside of the testes and ovaries. An entirely satisfactory explanation of teratomas is obviously not yet at hand. See the literature in appendix for theories.

In a number of teratomas, particularly of the testes (Pick and others), more rarely of the ovaries, there are microscopic chorionepitheliomatous growths, in part typical, *i.e.*, made up of syncytium and elements which resemble Langhans cell layers, and in part only relatively similar, *i.e.*, which show only here and there a syncytium; and furthermore there are occasional microscopic hydatidiform mole-like structures. Schlagenhaufer believes the former arise from fetal villous epithelium, and those like hydatidiform moles he regards as true moles. On these grounds he has even made up a genetic differentiation of teratomas into those which contain either egg structures or their derivatives and those which do not contain these structures; the first-named have their genesis in polar cells, the last in misplaced blastomeres. But these deductions have been much disputed and most authors believe with Risel (lit.) and others (Schmeel, Klotz) that the chorionepithelioma-like growths in teratomas have nothing to do with the malignant chorionepitheliomas of the woman, but are merely the ectodermal components of the teratoma, *i.e.*, a particular form taken by the fetal ectoderm which can give rise to the most varied forms of structures. But doubts have also been expressed against this explanation (see pp. 1509 and 1587). Occasionally, as in the cases observed under "testes" (p. 1507), the growth is unilateral in its chorionepitheliomatous form. The author saw such an ovarian tumor weighing 3400 grams, and producing many metastases in the liver and lungs. The hydatidiform mole-like structures as described, do not withstand a critical microscopic examination; there is only a superficial similarity between the tags of true hydatidiform moles and these intravascular floating tumor nodules. Moreover, there occur grape-like tumors in other situations, such as the cervix and in the bladder (see under those parts). L. Loeb may be consulted for other conceptions regarding the growth of chorionepitheliomatous-like formations in the ovary, and p. 1509, under testis, may be consulted for those in the testes.

The cysts so regularly found in teratomas are lined partly with squamous epithelium, partly with cylindrical epithelium, and also with flat cells similar to those lining lymph cysts (see p. 1583). According to Bandler, there are transitions between the various forms. Dermoid cysts are frequently found together with other cysts, see p. 1568. A general relationship to Wolffian bodies can hardly be believed (Bandler). If solid teratomas have a sarcomatous framework, they grow very rapidly and the metastases are sarcomatous; but in these cases it is necessary to differentiate between richly cellular mesenchyme parts which may also metastasize, and true sarcomas (see p. 1585). Carcinomatous degeneration may also occur; and sometimes a combination of both (Bukojemsky, Bottger). Teratoid, or, as Benda says, organized metastases also occur, just as they do from tumors in the testes (Kroemer, lit., Daels). In dermoid cysts there may be occasional peritoneal nodules as implantations of scattered cyst contents (fat, hair, sebaceous material); at times these are broken off pieces (Boxer) which must be differentiated from true metastases.

Animal Parasites.—Echinococci are very rare (Freund, Schatz, B. S. Schultze, Tittel). In the collection at Gottingen, there is an echinococcus of the right ovary as large as an apple; the left ovary shows a cyst.

Fallopian Tubes

The Fallopian tubes, according to Hofmeier, are about ten to fourteen cm. long. They are muscular tubes lined by a simple ciliated cylindrical epithelium thrown into many folds and rich in blood vessels. On cross section, the folds and plica in the tube appear like tags or papillae (these are artefacts, see p. 1559). Glands are not a part of the physiological structure of the mucosa, but in chronic salpingitis, glandlike structures appear from adhesions of plica and growths of the epithelium (see v. Franque). Lymph follicles are not present in the normal tube, but occasionally are found in chronic inflammation (Hedinger, Gutt). In senile involution, the muscle fibres disappear more and more, the wall becomes sclerosed, the cylindrical epithelium is flattened. (More details concerning connective tissue fibres in the tube by Horrmann.) The tubes take the ovum coming from an ovarian follicle during ovulation, and slowly carry it to the uterus by means of the cilia, or peristalsis, or both. During the passage of the ovum, the fimbriated end remains passive, and a large number of ova are lost into the abdominal cavity. The spermatozoa of the male may reach the fimbriated ends of the tubes quite quickly through contraction of the tube or through their own movements. The direction of movements of the ovum and spermatozoa are opposed in the tube. Impregnation of the ovum may take place in this situation; perhaps this is the normal event (see p. 1601); the impregnated ovum wanders into the uterus, but if it remains in the tube it leads to ectopic gestation. Some, on the contrary, believe that impregnation of the ovum in the tube always leads to tubal pregnancy.

Malformations of the Tubes.—Defects of the tube are usually associated with defects of the uterus and seldom occur by themselves. Accessory tube orifices are occasionally seen in the neighborhood of the fimbriae. Accessory tubes are not rare; they may be found on that part of the broad ligament between the tube and the ovary, on the stem of the tube, in the broad ligament, and between the leaves of the latter. They may have fimbriae, an open abdominal lumen and internal folds. They are pedunculated or not, without communication with the main tube. In accessory tubes with both ends closed, hydroparasalpinx as large as a child's head is said to arise, (Kossmann); but this view is doubtful (see Schickele). True double tubes, with or without double ovaries, are very rare (Bab, lit.). Schickele believes that small cysts lying around the posterior part of the tube are due to diverticuli, probably dependent on embryonal disturbances in Müller's tubes. According to Kroemer, diverticuli or blind pouches may occur in normal tubes also. There is much variation in the length and in the situation of the tube. The persistence of spiral winding depends on hindered development at the time of puberty, (hypoplasia of the tube); according to Freund, serious consequences may arise, such as tubal pregnancy, stasis of secretion and cystic transformation. The hydatids of Morgagni have been discussed on p. 1464 (see also Peters, lit.). They are pedunculated cysts with pedicles about as long as the fimbria of the tubes (Kobelt). Waldeyer believes they are secondarily formed blind pouches on the infundibulum, but Nagel believes they are the blind upper end of the Wolffian ducts; according to Kolliker, they are pathological structures, the result of lymphangiectasis. But other pedunculated cystic structures on the fimbria, on the tube, or on the ala vespertilionis, are often called hydatids of Morgagni. According to Kossmann, these are mostly accessory tubes; in part they are, however, cysts of the Wolffian ducts, and in part epoophoron cysts. Pedunculated structures connected with the fimbriated extremities of the tubes and of the broad ligaments have been considered by Roth as rests of primitive kidneys, but by Schickele as abnormally numerous coelom epithelial inclusions. Other small cysts on the tube, broad ligaments, ovaries and the vicinity are believed by some to be peritoneal epithelial cysts, and by others, germinal epithelial cysts. Further details of these small structures can be found on p. 1554.

Circulatory Disturbances.—The tube is influenced by similar circumstances which influence the mucosa of the uterus in inflammatory hyperemia; (probably the tube itself also menstruates). In active acute general peritonitis, the abdominal end of the tube is vigorously injected and reddened. In the stasis of heart failure, or in strangulation or torsion, the thickened edematous mucosa is blue red. In thrombosis of the ovarian vein, the walls of the tube and the ovary also are soaked with blood and swollen (hematoma or hemorrhagic infarction of the tube). Kermauner has described phleboliths in the fimbria.

Hemorrhages occur in inflammation (see under chronic salpingitis, p. 1592), and among other things, in phosphorus poisoning. Brown pigment remains. Larger collections of blood leading to hematosalpinx necessarily indicate that the abdominal end of the tube is closed, as, for instance, by perimetric adhesions; otherwise the blood would run out. Tubal hemorrhages may occur from pressure and tearing, as from tumors, *e.g.*, large myomas, or following menstrual congestion, and rarely in scarlet fever, typhus or cholera. In atresia of the genital canal (gynatresia, p. 1615) due to obstruction at the hymen, in the vagina, or in the uterus, the hematosalpinx has a very distinct significance (fig. 761, p. 1473); the higher the point of atresia in the genital canal, the greater the hematosalpinx. The blood which comes from the tubal wall and perhaps also that which is forced back from the uterus, fills the tube at each menstrual period so that it becomes a convoluted, sausage-like sac. This blood is usually syrupy, viscid, the color of tea or chocolate, it does not coagulate (according to Klebe because of the activity of the secretion of the tube) and can be differentiated from tubal pregnancies by these criteria. But in torsion of the pedicle and in hemorrhage following passive congestion, the blood in a hematosalpinx may be coagulated (Fritsch). Most cases of hematosalpinx, however, are tubal pregnancies (p. 1607).

The Fate of Hematosalpinx.—Perforation into the abdominal cavity or into the rectum or to the exterior may take place. The first may lead to a fatal acute peritonitis or to internal bleeding (in favorable cases it leads to retro-uterine hematocele). In torsion of the pedicle, necrosis occurs;

in infection, suppuration of the sac follows. Ogorek (lit.) has described spontaneous separation of the female adnexa from torsion.

Inflammation of the Tube. Acute and chronic salpingitis can be differentiated, and according to the character of the exudate, we may have a catarrhal or a purulent salpingitis. According to the situation of the inflammation it may be an endo-, a myo- or an interstitial salpingitis. An acute catarrhal salpingitis, which occurs particularly in the mucosa and especially at the ampullae, may be called an endosalpingitis; the mucosa is intensively reddened and swollen, the folds are thickened, infiltrated by cells, and covered with a turbid, gray mucus.

Abscesses in the walls of the tubes may break into the lumen and later be covered by epithelium which becomes snared off and shows as branched intramural spaces (Hohne). Kroemer and Maresch believe that, in these cases, the presence of preexisting tubal diverticuli have greater significance than ordinarily.

In chronic inflammation, the mucosa may be either atrophic or hypertrophic; changes in the fibromuscular coat play a part.

Hyperplasias of the mucosa with several layers of epithelial cells and even adenoma-like pictures which, however, are merely misplaced parts of the canal system, are found in chronic inflammatory conditions of all sorts (R. Meyer, Neu), among which gonorrheal, and others, particularly tuberculous processes, may be mentioned (see p. 1598). In such cases, the picture may be quite complicated by the growth of the epithelium, which shows irregular thick layers and much polymorphous degeneration, especially vacuolization; it grows into the tubal wall and is not particularly well marked off from the cellular infiltrated mucosa. On the other hand, papillary growths can also be found, and, as the experience of the author has shown, may be easily mistaken for carcinomatous changes (see also v. Franque). The most difficult pictures to interpret are those in which masses of epithelial cells are so closely packed that they appear to be solid, broad, polymorphous cellular carcinomatous nodules, as in a solid carcinoma, especially since they are sharply contrasted from the cellular infiltrated deeply staining stroma.

Many forms of chronic endosalpingitis lead to induration and shrinking of the folds. The inner surface of the tube becomes flattened. The muscularis in the catarrhal type is sometimes atrophic, and sometimes hypertrophic. In spite of atrophy, the wall, usually in the beginning, is markedly thickened by connective tissue growth (interstitial salpingitis, Martin); then the tube becomes quite elastic. If thickened plica grow together after loss of their epithelial cells, pictures arise simulating glands or follicles on cross section, (pseudofollicular salpingitis, Martin). Hemorrhagic salpingitis is a particular form of chronic catarrhal inflammation.

In **gonorrheal salpingitis,** Schridde found the cellular infiltration in the plicae; the walls and the contents of the tube are extraordinarily rich in cells of the lymphocytic series, in contradistinction to the leucocytic cells of streptococcic pus; he believed this finding of differential diagnostic importance, particularly in chronic cases in which gonococci can no longer be demonstrated. The specificity of these microscopic changes for gonorrhea, as stated by Schridde and Amersbach (see also Heynemann, Watjen), is not in agreement with the opinion of others (Miller, lit., Wolff, Neu, Ploeger). Huebschmann, who studied a six weeks old case of gonorrhea, found that the plasma cells played no part; he believes, therefore, that many plasma cells merely indicate a chronic inflammation brought about by a number of possible organisms. v. Franque named among these infectors, B. tuberculosis, streptococcus lanceolatus, or staphylococci. The value of the finding of plasma cells in acute and subchronic recurring cases must therefore be recognized with reservations (see Weishaupt). Adhesions of the plica to each other are very common and often lead to serious consequences, (sterility, tubal pregnancy).

Pick discovered an interesting finding, viz., that in old suppurative salpingitis, much of what macroscopically appeared like pus is a collection of doubly refracting substances in large clear cells (see p. 1344). The author confirms this finding (see also Schmincke and Arndt).

"Nodular isthmian salpingitis" (Chiari and Schauta) has been called by Kehrer, "interstitial nodular salpingitis," and by Orth "productive glandular nodular salpingitis." It occurs particularly at the uterine end of the tube, but may also reach to the middle (Maresch), and shows small globular thickenings which appear like fibromyomas. They consist of smooth muscle tissue containing large numbers of duct or gland-like branching outgrowths of the mucosa, accompanied or not by cellular lymphoid tissue, some in communication with the lumen of the tube; small cysts here and there may also be present. According to Chiari, they occur by reason of a chronic inflammatory process which affects primarily the epithelium, *i.e.*, the mucosa, and leads to overgrowths and inclusion; the muscle growth, which is very variable, is secondary. v. Recklinghausen believes they arise from persistence of misplaced primitive kidney tubules and that even the cellular structures come from the mesonephron, therefore they are congenitally determined tumors (adenomyomas of the tube). Pick and Kehrer dispute the genesis of the cellular tissue from primitive kidneys, since well known congenital kidney rests (epoophoron, paroophoron, etc.) are never accompanied by lymphoid tissue. On the other hand, it is certain that misplaced glandular epithelial structures do arise from Müller's tubes in the uterus, where they are of highly cellular structure. v. Franque, and many others, particularly Maresch, and Wallart, believe thoroughly in the inflammatory genesis, as does Chiari, particularly in a gonorrheal or a tuberculous origin (see also Bulius, Wallart, lit.). R. Meyer speaks of the condition as "adenomyosalpingitis," analogous to adenomyometritis, see p. 1662. Recently Lahm and Rosenberger (lit.) revised the theory of congenital origin, and state that they arise because of misplacement of the mesenchymic blocks from which the uterine mucosa is built (Keibel-Mall); the development of cellular tissue occurs because of the meeting of the epithelium of Müller's ducts, which is also present, with the misplaced mesenchymic parts. As a proof for this theory, it is pointed out that these adenomyoses of the tube take part vigorously in the decidual reaction, while ordinarily the tube takes very little part in this process. See also Frankl.

Etiology of Tubal Inflammations.—The routes by which inflammation reaches the tubes are (*a*) from the endometrium through the opening of the tube, (*b*) from the peritoneal cavity through the abdominal opening, and (*c*) from the lymph, more rarely the blood stream, in the tubal wall. In simple chronic catarrhs which lead to hydrops, the point of origin and the route by which the infection reached the tube can no longer be demonstrated. Severe suppurating forms of salpingitis are caused particularly by the streptococcus, during the puerperium, following an abortion, after intrauterine medication (tampons), but also, for instance, by influenza, pneumococcus blood infection, and so on, particularly in gonorrhea, even latent infection (Noeggerath). In these cases, the inflammation may lead to death by peritonitis; it may heal, or may lead to a pyosalpinx. While in the above mentioned cases the spread of infection to the tube occurs mostly from within the uterus, there are other cases in which the infection comes from the peritoneum, either, as is rare, in connection with appendicitis, or after operation which leads to pelvic peritonitis, or, what is quite common, in septic peritonitis spread from a puerperal lymphangitis. At autopsy, it can occasionally be demonstrated that the fimbriated end of the tube dips into the exudate, and so to speak, sucks up the infectious fluid. The tubes may also be infected from the ovaries or from the intestines. In septic phlegmons, the infection can often be traced through the tubal wall. It is remarkable, in various tubal inflammations, but especially in gonorrheal salpingitis, the passage of which, in many cases, can with certainty be followed from the uterine mucosa, that both the endometrium and the uterine end of the tube up to the ampulla (the favorite situation of all tubal inflammations) remain entirely intact; in these cases it must be assumed that the infection reached the tube by way of the communicating lymph vessels or over the surface and that the inflammation healed very quickly in the uterus and in the uterine end of the tube.

The Course of Tubal Inflammations. Perisalpingitis. Tubal Sacs

If a salpingitis does not heal promptly, or if it does not lead to a fatal peritonitis, it becomes chronic, and important consequences are many adhesions and fibrous thickenings of the mucosa, and narrowing or dilatation of the tubes from the stagnant exudate. Particularly in long standing gonorrhea, but also in other suppurative inflammations, perisalpingitis is very frequent along with perioophoritis and inflammation of the pelvic peritoneum, by which the organs become adherent and misplaced by adhesions. Perisalpingitis may be part of a general peritonitis independent of tubal inflammation, or may be secondary to inflammations of the uterus. The tubes themselves become kinked, tortuous and their abdominal ends are closed. The latter is essential in the development of a dilatation into a tubal sac which is filled by exudate from out of the wall of the sac. (Instead of the word tubal sac, A. Martin has suggested the name "sactosalpinx," qualifying it by the terms serous, hemorrhagic or purulent as the case may be.) The fimbriated ends disappear and the abdominal opening can no longer be found. At times, through kinking or "swelling" of the mucosa, the tube is obstructed at its uterine end, but this is rather uncommon. According to the contents, there are recognized hydro-, hemato- and pyosalpinx. The first two are consequences, *i.e.*, end stages, of a catarrhal inflammation; the latter is the end stage of a suppurative salpingitis. The tube, according to the degree of filling and the presence or absence of adhesions, becomes twisted, contorted, kinked, spindle-shaped, sausage-shaped or retort-shaped (fig. 818). Torsion of the pedicle is a common occurrence.

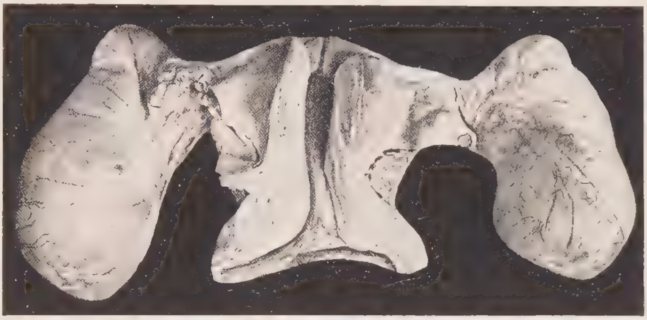


FIG. 818.—Bilateral hydrosalpinx from a syphilitic woman 45 years old (ulcer of upper lip, three small aneurysms of the ascending aorta); ¼ nat. size.

In hydrosalpinx, the abdominal end is obstructed but adhesions are usually few; in 137 cases, Martin found adhesions in 46. In the cases without adhesions the obstruction may be congenital or the result of chronic inflammation. The contents are clear, muco-serous or purely serous, (according to Jagerroos, lit. the serous contents in well defined cases are due to transudation). When the opening into the uterus is not obstructed, the internal pressure rises until the fluid contents, sometimes several hundred grams, are emptied into the uterus, whereupon such troubles as pressure, urinary difficulties and obstipation, are relieved, only to return as the fluid reaccumulates (hydrops tubae profluens). A hematosalpinx of inflammatory origin may arise from a salpingitis catarrhalis; the hemorrhage may be menstrual, inflammatory, traumatic or because of stasis in torsion of the pedicle. The contents are occasionally coagulated, but are usually fluid in contrast to the coagulated contents of a tubal pregnancy (Veit). In a pyosalpinx, the markedly contorted tube may reach the size of a fist or even a child's head. The wall, as well as the peritoneal covering, is tough and thickened, the mucosa is more or less infiltrated by pus (see p. 1592), and occasionally gone in older sacs. Sometimes a pseudomembranous diphtheritic salpingitis is encountered; adhesions among the plica lead to internal passageways and separated cavities (pyosalpinx saccata); in other cases compartments arise from peritoneal adhesions and fixation of the tube in a spiral position. Consequences: perforation may occur into the adhesions which are always present, and many sacs may arise, or into a neighboring organ such as the rectum or the ovaries; in the latter case tubo ovarian abscesses appear. The pus may become thickened and calcified, or may disappear and a serous fluid remain.

In chronic inflammation of the tubes (gonorrheal, tuberculous) a large percentage of cases shows small cell infiltration of the outer layers of the appendix (Moritz), but Schridde declares that salpingitis is uncommon in appendicitis.

Bacteriologic findings in tubal sacs: the pure watery contents of a hydrosalpinx are bacteria free. But even the pus in an older pyosalpinx may be sterile. When bacteria are found they are apt to be gonococci, streptococci, more rarely staphylococci, colon bacilli, pneumococci, influenza bacilli and others (Kisskalt). In the 206 cases investigated by Wertheim, gonococci were found 56 times, streptococci 11 times, and staphylococci 4 times; in 122 cases the tubal contents were sterile.

Tubo-ovarian Cysts.—The following theories are offered for the genesis of these cystic sacs which often take the shape of a retort; the walls are made up in part from the ovary and in part from the tube:

(*a*) The fimbriated end of the tube has become adherent to an ovarian cyst which has later emptied itself into the lumen of the hydropic tube (Richard). The cyst may be a normal or a hydropic follicle, a corpus luteum cyst, a cyst adenoma, etc. (*b*) When the walls of a hydrosalpinx are in connection with the walls of an ovarian cyst, disappearance of the partitions will effect a communication between the two cystic cavities (Veit); this view is accepted by Orthmann, and more recently by Preiser for the great majority of cases. (*c*) The fimbriated end of the tube slips into a ruptured ovarian cyst and the walls grow together (Burnier). According to Pfannenstiel, it is possible that a peritubal pyocele develops from the exudate surrounding a tube, forming an encapsulating membrane which encloses the tubal end and thus separates the tube from the cystic ovary. After disappearance of the wall between the pyocele and the ovarian cyst, there is left a tubo-ovarian cyst with early purulent and later serous contents. According to Zahn, however, the process is merely like that of an hydropic tube, which is differentiated from the ordinary form of hydrosalpinx only in that the ovary is enclosed in the cyst wall by the obstruction of the abdominal end of the tube, just as though a stone had been forced into the wall of a sac. Tubo-ovarian cysts seldom reach large size, since the open uterine end periodically empties the contents; there have, however, been cysts as large as a child's head. If the fimbriated end of the tube surrounds the normal ovary in such manner that part of it lies in the infundibulum, there arises a so-called ovarian tube. If a pyosalpinx ruptures into an ovary, a communicating pus cavity, a tubo-ovarian abscess is formed. On p. 1602 the relationship to extra-uterine pregnancy is discussed. The literature concerning the rare carcinomas of tubo-ovarian cysts is discussed by Orthmann.

Infectious Granulation Tumors.—Tuberculosis is the most important of these. It is met in connection with tuberculosis of the endometrium (fig. 819) or as an isolated condition; in the former, the tubal involvement is usually found in a later stage than that present in the uterus. According to v. Franque, the Fallopian tubes are involved in fully 90% of the cases of genital tuberculosis. Ordinarily both tubes are involved. In the acute stage, the swollen, reddened mucosa folds are covered with pus or caseous material and infiltrated by gray miliary nodules. In the chronic stage, the twisted tube is thickened, tough, and the internal walls are caseous. The lumen remains as an irregular cavity or is filled with caseous material. When the contents are voluminous and suppurating, the tube enlarges after obstruction of the abdominal end, and occasionally becomes as thick as an arm and is pulled out into a long sac (tuberculous pyosalpinx). Frequently, however, the abdominal end is open and the contents are spread to the peritoneum. The author saw the peritoneum involved in 60% of the 32 cases he studied. Adhesions are very frequent.

As an early stage, Simmonds described a bacillary catarrh (see p. 1516). Voigt (lit.) described a reactive growth like carcinoma in the mucosa (Kraus, v. Franque); the differentiation between this epithelial overgrowth and carcinoma is often quite difficult as the author can testify (see p.

1605). Frist saw an adeno-like form, while Gaifami (lit.) described the more rare papillary growths.

The contour of the swollen tube is like that of a sausage, a club, a retort, or a rosary; the latter form, however, is not sufficiently common to make it of diagnostic importance as once considered. The narrower parts of the tube are, as a rule, much less involved. According to Hegar, the nodes as described in isthmian salpingitis nodosa (p. 1593) are quite frequent in this form. The consistency of the tube is usually doughy. The outer layers are thickened by connective tissue overgrowth, but parts of the wall may be thin; hernia-like protuberances are forced through and become filled with caseous pus: the author observed such nodules as large as a cherry.

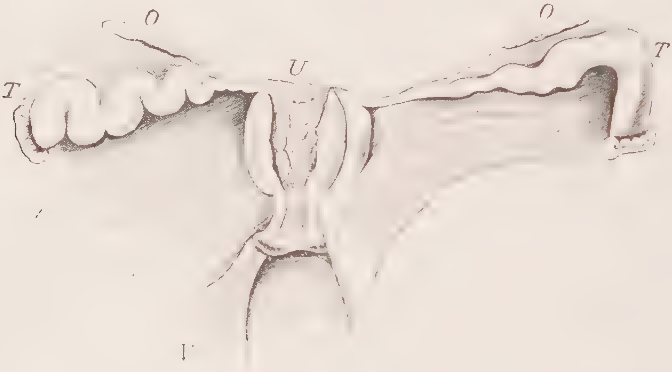


Fig. 819.—Tuberculosis of genitalia of a girl 5 years old; caseous salpingitis and caseous endometritis (with many bacilli); many miliary tubercles of vagina. Cervix, body and os uteri microscopically free; likewise ovaries; but tuberculosis of lungs, intestines, peritoneum, bones of hands and feet, lymph nodes, tuberculous basal meningitis, granuloma l. knee (osteal form, with area as large as a cherry perforated from the lower epiphysis of femur between the condyles into the joint); 4/5 nat. size.

Etiology. Tuberculosis of the Fallopian tubes may be primary, as many assume, but anatomically this is difficult to establish, and is infrequent. According to Hegar's clinical experiences, which have, of course, been disputed by other clinicians (Blau, see also Müller), and pathologists (see B. Simmonds), this is the most frequent form of primary genital tuberculosis in the woman; tubercle bacilli are said to pass through the vagina and the uterus (coitus, instruments, finger) and to reach the tubes without leading to changes in the endometrium. (The possibility of such an ascending tuberculosis has been demonstrated experimentally by Jung and Bennecke, and confirmed by Hashimoto.) But v. Baumgarten believes this is a questionable physiological way; (see also the experiments of Blau, and those contrary, Jung, Engelhorn, Thorn, Bauereisen). Peritoneal and uterine tuberculosis may manifest themselves at a later time. As a rule, however, the involvement of the Fallopian tube is secondary to that of the lungs, intestines, peritoneum, bones of the pelvis, and occasionally to general miliary tuberculosis. We therefore see a hematogenous origin as well as an origin by direct continuity from the neighborhood, as from the peritoneum, the intestines, or from the urinary tract. Kafka (lit.), in very early cases, thought he could demonstrate histological differences between tuberculosis of the tube arising by continuity in which he found the tubercles particularly in the mucosa, and tuberculosis coming through the blood stream, in which he found the tubercles in the middle part of the wall of the tube. As an example of hematogenous tuberculosis of the Fallopian tubes, the route which is now thought to be by far the most frequent (Kleinhans, Amann, Graefe and others), the following case in an eighteen year old virgin may be cited. Both Fallopian tubes were caseous, and a very small caseous mass was found in the endometrium; there was, however, no other evidence of the disease in the entire body except a small, thoroughly encapsulated, sub-pleural fibro-caseous mass as large as an almond in the right lower lobe of one lung, and a fibro-caseous bronchial node on the right side with two scars of bronchial fistulae. The author might mention three further observations as follows: 45 year old women, obsolete tuberculosis of the lungs, isolated tuberculosis in a tube as thick as a small finger; 29 year old virgin, old caseous tracheobronchial lymph node, bilateral caseous tuberculosis of the tube and of the uterus (distinct giant cell tubercles); seventeen year old virgin dying of cardiac decompensation following articular rheumatism, small caseous mass in the lower lobe of the right lung and in the bronchial lymph nodes of the right side, bilateral caseous tuberculosis of the tubes, nodules in the endometrium and in the pouch of Douglas. Such cases illustrate the fact that when such hidden primary foci are present, the false clinical diagnosis of primary tuberculosis of the tube may easily be made; without a careful autopsy such diagnoses have little value (see also Weinbrenner). Cohnheim had already pointed out that infection of the tube was a common occurrence in tuberculous peritonitis (see also Kundrat), and v. Franque (lit.) believes that this mode of infection is of equal importance with that coming through the blood stream. Secondary tuberculosis of the peritoneum from the tube is more frequent than secondary infection of the uterus; a tuberculous suppurative peritonitis, even a phlegmonous peritonitis, may follow such tubal infections, and it has been repeatedly shown in these cases that there is often mixed infection with gonococci. The tuberculous suppurative peritonitis is occasionally limited to a small encapsulated part of Douglas' cul de sac; the author has seen many such cases in which the tubes lay in a saccular mass and many fistulae into the rectum communicated with the sac. This state of affairs is illustrated in fig. 851 (see also Piotrowska, Roux). Caseous infiltration of the ovaries, as well as of ovarian cysts and tubo-ovarian cysts, is not uncommon. General miliary tuberculosis coming from a tubal tuberculosis has been observed following child birth or miscarriage; the inner surface of the uterus may be coincidently involved (lit. by E. Kraus).

Michaud, Strong, Lehmacher have described the formation of bone in these necrotic, perhaps tuberculous, Fallopian tubes.

Both **actinomycosis** and **syphilis** are very rare in the Fallopian tubes. In the case of Zemann, (actinomycosis), the tube was transformed into a big convoluted pus-containing sac, the mucosa of which was infiltrated with yellow, fatty, actinomycotic granulation tissue; (Goldner, Schlagenhaufer, Hedinger, Brandenstein, lit.).

Tumors.—Primary tumors are rare. In the fibro-muscular coat there have been found: fibromas, fibromyomas, adenomyomas (Muskat), and sarcomas; in the mucosa there have occurred various types of new growths with papillary structure, such as polyps, fibroepitheliomas, carcinomas, which may be bilateral and similar histologically to the papillary carcinomas of the uterus and ovaries, (lit. Peham, Benthin, Boxer); they are particularly malignant (Kehrer, lit.); furthermore there have been described: sarcomas, sarco-carcinomas and other mixed tumors, thus carcino-sarcoendotheliomas (v. Franque). Lymphangiomas are quite rare (Kermauner, lit.). Carcinomatous tubo-ovarian cysts are rare (p. 1597). Even the malignant chorion epithelioma has been found in relation to a tubal pregnancy (Marchand-Ahlfeld and others, Risel, lit. Jeanneret, lit. Rossier, lit.) and has usually been discovered at operation. v. Franque particularly, points out the frequent occurrence of metastases in the uterus from malignant tumors of the tube.

Teratomas are very rare (lit. Orthmann). See under adenomyomas of the uterus (p. 1661) concerning adenomyomas of the tube and also under salpingitis isthmica nodosa (p. 1593).

Secondary carcinomas come from the ovaries or the uterus, but also *e.g.*, from carcinoma of the stomach which has spread to the peritoneum. There may be growth by continuity, or by implantation of the cells on the serosa of the tube; (concerning the much more frequent secondary ovarian carcinomas arising by this mode see p. 1577). It is rare to have a mucous implantation through the abdominal opening of the tube. The author observed a case in a 59 year old woman with colloid carcinoma of the pylorus which had spread to the duodenum with thick infiltration of the omentum, nodular and diffuse peritoneal metastases, particularly on the anterior parietal wall, and a few small colloid nodules in the small ovaries; both tubes were changed by large masses of carcinoma until the tube resembled a cornucopia; bloody softened carcinomatous masses bulged from out the ampulla. The author also observed retrograde transport by way of the lymph channels into the tube, as in the 54 year old woman mentioned on p. 1390. Sitzenfrey believes it is possible for small masses of uterine carcinoma to be pushed through colicky contractions out of the uterus into the tube and become implanted in this structure.

The literature concerning tubal new growths can be found by Peham, Doran, Orthmann, Kundrat, Schottlander, and in the appendix.

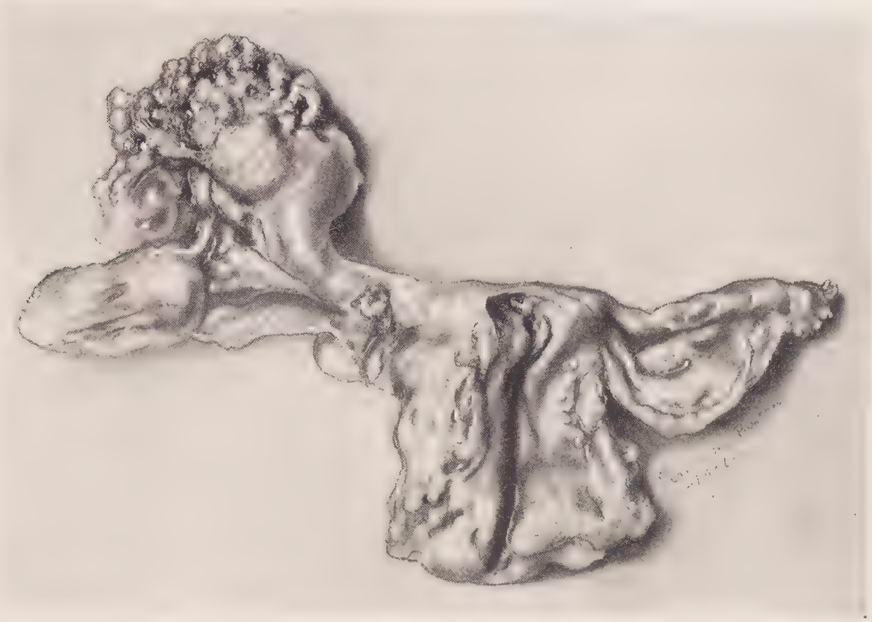


FIG. 820.—Primary carcinoma of the Fallopian tube. Operative specimen. L. H. #75. ½ nat. size.

Parasites.—It might be mentioned that oxyuris may reach the peritoneal cavity through the tube (see p. 855). Doleris described a unique case in which there were many large echinococci in both tubes.

Extrauterine Pregnancy

The impregnated ovum occasionally—probably not so rarely—does not become imbedded in the uterus, but elsewhere, in the majority of cases in the tube, rarely in the ovary, and perhaps never primarily in the peritoneal cavity. A placenta is developed at the place where the ovum sends in its allantois.

Coincident extra- and intra-uterine pregnancy is very rare (Nillson, Pernice, lit.), but recurring extrauterine pregnancy is not so rare (Smith). The situation of normal impregnation is, in all probability, in the ampulla of the tube or even between the tube and the ovary (see R. Meyer), and from here the egg wanders in a certain time (perhaps ten days, see Grosser) into the uterus where it is imbedded in the mucosa. Every normal pregnancy is therefore in this sense a tubal pregnancy (Waldeyer-Jossel).

The causes leading to hindrance in the migration of the ovum into the uterus may be summed up as follows: (*a*) loss of the ciliated epithelium of the tubal mucosa following old catarrhs; or loss of peristalsis and forward propulsion of the ovum. But many have found no trace of catarrh, in fact, a normal tube. In such cases it is possible that the ovum was impregnated and had reached a certain degree of development in the tube on the other side; after its passage was delayed, it became imbedded in the other tube rather than in the uterus. Incompletely developed or absent cilia in the isthmus of the tube is, however, typical of true hypoplastic Fallopian tubes (Hohne, lit.). (*b*) Immovability of the tube following congenital disturbances in its length or persisting infantile contortions (Freund),—but Hohne believes this is not enough to explain the condition; or kinks or pelvic peritonitis with adhesions; the spermatozoa may travel up the narrow tube but the ovum after impregnation cannot reach the uterus. But, on the other hand, such adhesions readily follow tubal pregnancy, and in many cases the above named factors cannot be found. If the pregnant tube is closed toward the uterus, the spermatozoa must have reached the tube and the ovum through the other patent tube (external wandering of the spermatozoa), an occurrence which newer investigations have shown to be not at all unusual (H. Bauer, lit.), even though the spermatozoa are phagocytosed in a few hours in the abdominal cavity (the very latest in 20 hours, Hohne and Behne); or the impregnated ovum (see p. 1474) wanders around in the outside, a condition which is probably the exception (see Burkhardt). (*c*) Opitz believes the most important factors in extrauterine pregnancy are disappearance of the mucosal plicae, adhesions between neighboring plica and branching of the folds, just as we see so constantly in inflammations. By these and because of inflammatory heterotopic epithelial growths, the wandering ovum is stopped (see also Hohne). (*d*) Micholitsch, on the other hand, believes the cause of tubal pregnancy is lodgment of the ovum in congenital blind passages, in diverticuli or in acquired accessory spaces in the tube, which are met sometimes as numerous adenoma-like branched spaces; it grows within those passage-ways and diverticuli (see p. 1605, Hohne and others). Kermauner (lit.) and others, doubt, however, that Micholitsch, Fellner, etc., have really demonstrated embedding in diverticuli. But v. Franque and Garkisch have undoubtedly demonstrated such possibilities. Huffman believes the most important factors are congenital anomalies in the tube, inasmuch as they predispose to unfavorable embedding places for the ovum. (*e*) Other factors such as mucosal polyps, myomas and so on, as mechanical hindrances, are but seldom a cause of tubal pregnancy (Hohne, Lahm, Lehmann).

Forms of Extrauterine Pregnancy.—There are differentiated: (1) **tubal pregnancy** which is further differentiated into (*a*) propria or isthmic, situated in the middle part, the most common form. Perhaps adhesions among the folds following previous inflammation are important in this form (p. 1592). (*b*) Interstitial pregnancy is quite rare (lit. by Werth, Raschkes, Weinbrenner, Wagner). The ovum is developed in that part of the tube lying within the uterine musculature, and narrowing of the uterine part of the tube may be the cause; see Runge. If development of the ovum takes place at the same time in the uterus, there arises the so-called tubo-uterine pregnancy. Occasionally, in interstitial pregnancy, rupture takes place into the uterus and the ovum enters this organ, but usually rupture is external. This must not be confused with pregnancy in a uterine diverticulum (p. 1617), when the tube is intact. (*c*) In pregnancy in the ampulla, which is fairly common, there are two varieties, tubo-abdominal, in which a part of the ovum bulges out into the abdominal cavity through the fimbriated end, but the placenta always, even if only slightly, is connected with the mucosa of the tube; the second variety is the very rare tubo-ovarian pregnancy which occurs in an ovarian tube or in a tubo-ovarian cyst (see p. 1597), into which a ripe follicle has ruptured. Pregnancy very rarely occurs in an accessory tube (Walthard, lit.) or in the stump of a tube (Diemer). An intraligamentary tubal pregnancy occurs when the impregnated ovum grows between the leaves of the broad ligament while the placenta remains attached in the Fallopian tube. According to Schuchardt, the maternal parts may be built in part from the musculature of the tube or from only the peritoneum of the broad ligament, and the wall of the tube is pulled out opposite the place where the ovum is imbedded. Very rare indeed is simultaneous pregnancy in both tubes (Laurell). (2) **Ovarian pregnancy** is very rare (lit. by Freund, Thome, Busalla, Mitchell, Bondi, see also Beneke, Beitzke). There are two varieties: (*a*) the ovum as it leaves the follicle may be stopped in a niche or a depression of the albuginea or inside of a larger depression in the epithelium of the ovarian surface (Hohne, Hannes), and be impregnated by spermatozoa in this situation (superficial ovarian pregnancy). (*b*) The ovum does not leave the follicle when it ruptures, but is impregnated in the theca folliculi by the spermatozoa (intrafollicular ovarian pregnancy). The deciduae is supplied by the granulosa. Imbedding of the ovum takes place as in the tube (Franz). The pregnancy may reach its normal completion, or the sac ruptures previous to this; hemorrhage then occurs, and the products of conception enter the abdominal cavity.

If it develops further, there arises a secondary abdominal cavity pregnancy (lit. by Leopold, Futh). Engelking (lit.) has described the rare intraligamentary ovarian pregnancy. (3) **Abdominal pregnancy**; the impregnated ovum is fastened on some part of the abdominal cavity; the latter then builds the serotina and becomes the site of development of the placenta. This occurrence is in all probability very rare (lit. by Werth, Jarzeff, Crotti, Hammacher); others believe it is entirely impossible (as for example Veit), or consider these cases as only secondary, or better, false, abdominal pregnancies in which the ovum or the products of conception have been forced out of the tube or ovaries. But newer investigations, particularly those of Richter, of Koehler, Walker, Reifferscheid and others have brought forth evidence for primary abdominal pregnancy. In other cases the abdominal pregnancy is merely partial (tubo-abdominal). It is interesting to note in the cases in which the rupture of the tube takes place in later months, and the rupture does not involve the placenta, that the fetus outside of the amnion may lie free between the intestines and remain living for a month (Harris, lit.).

Bruno Wolff (lit.) undertook experimental investigations concerning the development of extrauterine pregnancy.

The Reaction of the Uterus in Extrauterine Pregnancy.—The uterus becomes hypertrophied and a decidua is developed with three layers, just as though the pregnancy were in the uterus. The younger the pregnancy and the nearer to the uterus the ovum is placed, the more outspoken are most of the changes in the mucosa and the musculature of the uterus. The breasts also undergo hypertrophy. Occasionally the mucosa may not react until later. The surface and the glandular epithelium of the uterus may show syncytial changes (M. B. Schmidt). The decidual changes reach to the upper third of the cervix (W. H. Schultze). Enlargement of the uterus ceases after the fourth month. If the extrauterine pregnancy is terminated, the uterus regresses and the decidua is expelled, at least in the later months, usually in toto as a three layered, outer raw, tag-like sac with an internal smooth, wavy surface which has a hole in every corner. Occasionally the expelled uterine decidual sac is turned inside out (Buche). If the tubal pregnancy is interrupted very early, (four to five weeks), the decidua in the uterus may possibly regress in loco (see p. 1632).

Tubal Pregnancy, the Most Frequent and the Most Important Extrauterine Pregnancy.—It was formerly assumed that the reactive formation of a decidua developed at the situation where the ovum was fastened to the mucosa of the tube. According to the work of Kuhne, Griffiths, Aschoff, Heinsius, Futh, this does not occur, or at least in but very small amounts during the first month (Lange, and others, lit. by Aschoff); if a decidua is formed, it develops only in later months as a true decidua, and practically never occurs at the site of the placenta; a decidua serotina is, however, never developed. The ovum does not find suitable nutrition in the tube, and attachment of the ovum, *i.e.*, the development of the placenta, takes place by the embedding of fetal villi into the mucosa and the muscularis of the tube (Futh). While most authors do not believe there is a decidual reaction at the site of the embedding of the ovum, nevertheless v. Franque and Garkisch have demonstrated its occurrence in an observation they have recently made. According to Webster, Orthmann, Kuhne, Voinot, Couvelaire, Durante, Mandl, Lange, Wallart, decidual changes in the tube as well as in the uterus in tubal pregnancy take place only in focal situations. It must, however, be emphasized that there is a very rich cellular infiltration from the chorion which enters the bordering uterine tissue so thickly that it may easily be misinterpreted as a decidual change. As a matter of fact, just as in the uterus, (Siegenbeek van Heukelom), the growth of fetal epithelial villi proceeds to the form of a sort of second shell around the egg wall, a "suction plate" (Aschoff), which is supported by the villi (see Zedel), and which also opens the vessels of the mother to the establishment of a placental circulation. This invasion and destruction may progress to the serosa. This ever increasing growth of fetal cells, which brings about slow destruction of the wall of the tube, is hidden through organization of blood clot or through fibrinous exudate with subsequent fibrous change and thickening of the serosa. Werth differentiates a columnar and intercolumnar embedding of the ovum. The latter, which is the more common, occurs in the mucosa between two folds; in the former the ovum rests upon the height of a fold or between the secondary folds of a principal fold. The chances of abortion because of the small amount of surface, is naturally much greater in the columnar form. In the intercolumnar form, on the contrary, the wall of the tube in which the ovum is embedded is more prone to rupture. Hohne differentiates internal rupture, (rupture of the tube). In the most frequent site of embedding of the ovum, *i.e.*, in the ampulla, it is easier to have rupture internally toward the remainder of the lumen of the tube (abortion); in impregnation, or rather embedding, in the isthmus, the walls of the tube are destroyed by the eroding ovum (rupture); when the ovum is embedded in the middle part of the tube where the dissolving of folds and the epithelial walls occurs, abortion and rupture are equally frequent. As the ovum develops in the walls of the tube, not only the mucosa, but also the smooth musculature attempt to surround it. The capsule or pseudoreflexa so formed is infiltrated during the further months of pregnancy by the growing masses of trophoblast from the growing ovum, or it is destroyed by hemorrhages (Voigt). These unfavorable circumstances explain the readiness with which the tubes rupture, or with which an abortion occurs; tearing occurs during the first part of pregnancy, naturally only at the site of the placenta. On the other hand, the blood vessels embedded in the fetal tissue are particularly prone to be torn, especially through contractions of the tubes. The hemorrhages lead further to rupture or to tubal abortions. While the musculature of the tube at the situation of the placenta is much thinned or disappears entirely and is replaced by peritoneal scar tissue, in the remainder of the tube, it is occasionally hypertrophic, probably because of contractions stimulated by the ovum, particularly the dead ovum.

Fate of Tubal Pregnancies.— As a rule pregnancy is terminated during the first three months, mostly during the second. This is caused:

By rupture of the tube externally with hemorrhage and with or without release of the ovum. This seldom occurs later than in the third to the fourth month, and is most frequent in the sixth to the eighth week. Rupture is more frequent when the egg is embedded in the proximal (uterine) part of the tube. Causes: increasing thinness of the tube where the fetal villi grow into its walls and tear them apart, muscular contractions and trauma such as tearing and jars, as during coitus. The contractions may occur not only in the convexity produced by the stretching of the muscles where the ovum is embedded, but as Fehling assumed, in normal parts of the tube also; as the ovum is forced by colicy spasms against the yielding parts of the tube, it ruptures both at the thick and thin places. According to Orthmann and Martin, rupture is usually secondary to hemorrhages at the site of the placenta, between the membranes and the ovum; this may occur during increased blood pressure as in menstruation, or after lifting heavy weights, etc. The tear through which the blood escapes is often very small; it may be only as large as a needle. Occasionally the tear is larger; it takes place at the site of the placenta, and tags of chorion mixed with solid blood coagula prolapse through the place of rupture. Bleeding may be very marked and occur from both arteries and veins; in the so-called "fulminant" hemorrhages (see under peritoneum, p. 861) the blood comes from the intervillous spaces into which the arteries open directly (see also Taniguchi). Tears from small openings occasionally become larger by sudden swelling of the ovum by hemorrhage; the elastic sac of the ovum may be preserved, while in other cases rupture of the membranes occurs and the products of conception, or perhaps even the entire ovum, much stretched by hemorrhages into the egg chamber, are expelled through the tear, which may then be opposite the site of attachment of the placenta. The ovum may, however, remain in the tube. Kiutsi differentiates between rupture—acute rupture of the capsule—and slow erosion—chronic rupture of the capsule.

Consequences of rupture may be (1) acute internal fatal hemorrhage (see p. 861); (2) the formation of an encapsulated mass of blood as a retrouterine hematocele or a hematoma (following intraligamentary rupture); or (3) complete healing, resolution.

Fate of the products of conception. The ovum may die long before rupture takes place; if not, it usually dies at the time of rupture. In rare cases, life is spared after the ovum escapes through the tear into the abdominal cavity, provided the placenta remains attached in the tube. Then there results a secondary abdominal cavity pregnancy. If the ovum dies after rupture, it may remain in the tube or may reach the abdominal cavity; in these places it may be absorbed without trace; when complete healing has taken place it means that the tubal deciduae, the uterine deciduae and the hemorrhage are all entirely absorbed. As a rule, however, there develops a retrouterine hematocele (see p. 1608), in which there are found chorionic villi covered with blood and perhaps the body of the fetus also.

Tubal pregnancy may be terminated by abortion, and death of the products of conception; this is the more frequent event, and usually the more benign in consequences. Abortion is more likely to occur when the ovum is embedded in the distal (abdominal) end of the tube, from hemorrhage between the ovum and the site of the placenta. The hemorrhage is from vessels in the mucosa which are lying in the region of the fetal chorionic cell growth and which tear from sudden increases in blood pressure or from contraction of the muscles in the tube. According to Aschoff, those vessels in the swollen mucosa and the muscularis which help to build the pseudoflexa are particularly endangered. The ovum is thus killed. Hemorrhage may even occur into the ovum itself. The further changes vary: abortion may take place into the tube and the dead embryo be quickly absorbed, while the amnion, and particularly the chorion, with whole nests of Langhans cells inside of the maternal tissues (Heinsius) remain for a longer or shorter period mixed in with the blood coagula; they may actually distend the wall still further and lead to late rupture (see Aschoff, lit.). Collections of blood (hematomas) between the ovum and its covering cover the ovum completely. Sometimes the ovum is released by the hemorrhage and forced in toto from the fimbriated end of the tube out into the abdominal cavity while the chorion remains behind, (complete tubal abortion); or the fetus alone is forced out with blood, and may later be encapsulated in some situation in the abdominal cavity; or nothing but blood escapes into the abdominal cavity from the tubal opening while the ovum enclosed in a clot remains as a blood mole (incomplete tubal abortion). The early death of an ovum leads to hemorrhage internally, *i.e.*, into the abdomen as well as externally from the uterus. The latter occurs quite independent of the expulsion of deciduae; indeed, the uterine deciduae often undergo regressive changes in loco. In these cases, bleeding into the abdominal cavity is usually intermittent and leads very often to a hematocele. Death from hemorrhage in tubal abortion is rare, as might be expected from the above mentioned anatomical considerations. Schiffmann, (lit.), has written of the final, infrequent spontaneous healing of extrauterine pregnancy through resorption and organization of the products of conception of the young ovum.

Retro- or Periuterine Hematocele.— The hemorrhage following rupture, or tubal abortion is usually more severe the older the pregnancy. Rapid death of the mother may take place from violent bleeding into the free peritoneal cavity. In other cases, a retrouterine hematocele usually, even if not always, (see pp. 1548 and 1552), is caused by an extrauterine pregnancy, chiefly tubal. The hemorrhage, however, may take place between adhesions and into connective tissue pseudomembranes which are quite commonly the result of tubal pregnancies or previous pelvic peritonitis, and which cover Douglas's cul de sac. If the placenta develops in the region of the mesosalpinx and hemorrhage begins, the blood may force itself violently between the leaves of the broad ligament (intraligamentary hematoma). These above mentioned conditions are, however, not necessarily needed to produce a typical hematocele; rather it occurs in some such way: hemorrhage from out the tube follows either tubal abortion or tubal rupture (Lindenthal); the blood is not scattered, but mixed with fetal elements, is collected in Douglas's cul de sac and coagulated, possibly because its coagulative ability is increased (Heinsius), or because its absorption is hindered by previous primary changes in the pelvic peritoneum (see Busse). The neighboring organs such as coils of intestines, posterior wall of the uterus, omentum, broad ligament, etc., surround the mass of blood, become adherent, and the serosa undergoes inflammatory changes and overgrowth. Then new blood is added (characteristically accompanied by pain). The blood may find a cavity covered by young connective tissue which is then distended further. At all events, there appears a spherical tumor-like mass of blood varying greatly in consistency, and reaching the size of a man's head by the accession of more masses. The process therefore is organization of a hemorrhage in the free peritoneal cavity (Maennel), but even large hematoceles may disappear spontaneously. Occasionally a compact shell of fibrous and connective tissue is developed around the periphery of the coagulum (in months). Such an hematoma may be shelled out in toto; it is often called an "encapsulated hematocele" or a "solitary hematocele" (Sanger). Rupture of an hematocele through the rectal wall or posterior wall of the vagina is not uncommon when suppuration or phlegmon is added by infection from the intestines or from a previous infection in the tube (see Kustner).

The Rarer Fates of Tubal and Ovarian Pregnancies.—Exceptionally, a tubal pregnancy goes on to normal term. According to Lichtenstein, this is because of growth of the villi into the richly vascular connective tissue of the mesosalpinx; placentation is "basiotropic" which means directed toward the base of the organ, in contrast to those which are directed toward the surface, and in which perforation occurs quite commonly. If an ovarian pregnancy goes on to the second half of term or until the end, placentation has taken place toward the hilum. As a rule, the products of conception are grown fast to the neighboring organs through many adhesions. The amniotic fluid is usually small in amount, and malformations such as club feet, torticollis, and others are quite frequent. If operative help is not at hand when the fetus reaches term, the fetus dies because the placenta becomes loosened; this is followed by hemorrhage and expulsion of the uterine deciduae. Contraction of the tubes and of the broad ligament may then lead to rupture and to hemorrhage. Peritonitis may likewise follow. The fate of the products of conception are: (*a*) the contents may remain aseptic, the amniotic fluid be absorbed, the large amniotic sac become smaller and cover the fetus as with a cloak. Connective tissue may tightly enclose the structure on the outside. After many years the placenta disappears in the amniotic sac. Mummification of the fetus takes place, which may finally become a lithopaedion, (pure mummification is called dermatopaedion, see Kroemer). If the cloak is impregnated with calcium salts the structure is spoken of as a lithokelyphos (Kuchenmeister). If the amniotic sac and the superficial layers of the fetus adherent to the amniotic sac become calcified, the condition is spoken of as lithokelyphopaedios. These have occasionally been observed in ovarian pregnancies also, (lit., Weibel). If the fetus is not covered by the membranes but is adherent to coils of bowel or to the omentum (as in the case of Biener), and if even the deeper layers are infiltrated by calcium salts, the condition is spoken of as lithopaedion, (stone child). According to the careful statistics of Strauss (lit.), the most common form is that in which the transformation to stone is not total, but only partial, in the form of a mummified petrifaction. Even in these cases the internal organs may still be recognized by their structure many years later. The cross striae of the muscles are preserved for particularly long times; the author saw striped tongue muscle in a lithopaedion from an 85 year old woman. The well known stone child of Leinzell (Kieser, I. Diss., Stuttgart 1854) was found in a 94 year old woman who had carried the structure for 46 years; see also the case of Vogt, lit. The cerebral substance and the blood often change to a pulp, rich in cholesterin. This diffused and changed blood coloring matter stains the lithopaedion yellow red. Such structures may remain, even for decades. Lithopaedions, as a rule, are found in the abdominal cavity and occasionally in the tubes (Kratzeisen). J. Werth has described a lithokelyphopaedion in the uterus. (*b*) Older sacs may be infected, probably from the intestines, and suppurate or undergo gangrenous changes. The fetus undergoes putrefaction and is macerated to the bones (skeletonization of the fetus). Fatal peritonitis, with or without rupture of the sac, may follow. More commonly, perforation of the sac into neighboring organs takes place after erosion. The watery contents of the macerated fetus, and even the bones may then be discharged piece by piece through the rectum, bladder, vagina (occasionally), or even through the external abdominal wall; in the bladder, stone formation has

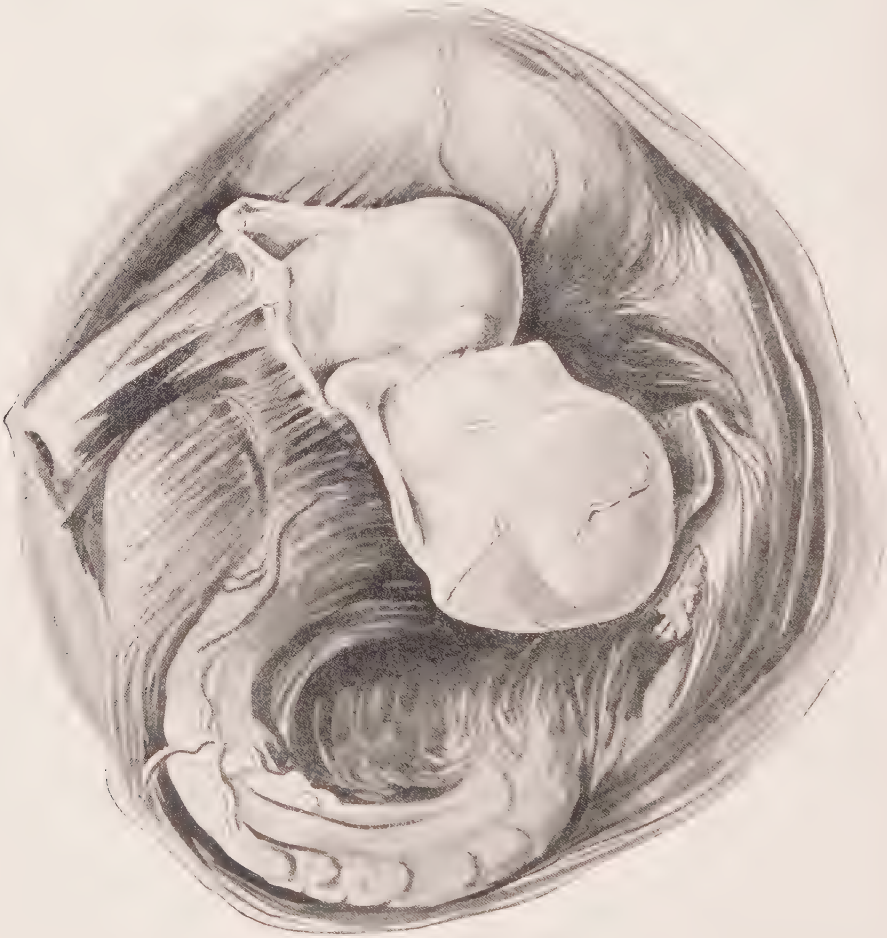


FIG. 821.—Lithocelyphopaedion from a woman 85 years old; drawn in situ; bladder in front, sigmoid behind; ¾ nat. size. (Details by Wallart, Z. f. B. 59, 1907.)

been known to follow. When everything is eliminated, which may take years, the sac shrinks and heals. Death, however, is much more frequent from the absorption of septic material. Skeletonization of the fetus in an aseptic closed sac has occasionally been observed (Emanuel).

Uterus

Changes in Position of the Uterus.—The exact importance of changes in position is of great gynecological interest. A short summary will be given here.

The normally quite movable uterus changes its position with different stages of filling of the bladder, the rectum, and with changes in intra-abdominal pressure. The muscle fibres in its ligaments, its own weight, the tension of the pelvic floor and the vagina guarantee its physiological position. In the upright posture with the bladder and rectum empty, the normal position is in anteversion. The axis of the body is horizontal; the cervix is bent in a curve, open at the front.

Pathological Changes in Position.—Changes in position of the organ are called pathological when they are stable; this is usually due to conditions outside of the walls of the organ. Thus the uterus may be pushed out from the true pelvis by a tumor (elevation), and by hypertrophy may become elongated; through relaxation of the parts fixed to the organ it may descend (descensus uteri). The pull of exudates or adhesions, a short broad ligament, etc., pull the uterus to the right or the left (dextro- and sinistro position). If the organ in toto, *i.e.*, with the cervix, is pulled by a more permanent force, *e.g.*, by a pseudo ligament, it is spoken of as rotation (Kustner); slight rotation to the right is physiological and is accentuated during pregnancy. When turned on its axis, on the contrary, there is a strong rotation of the body of the uterus, usually toward the right, while the cervix from which the turning takes place, remains fixed in its position. This is therefore sometimes spoken of as torsion of the cervix. Rotation takes place, among other things, in myomas, ovarian tumors, and so on. It may also be seen in a gravid or an involuting uterus (Glinski, lit., Vogt). A marked fixed angular kinking of the curvature of the cervical canal is called a pathological anteflexion; fixation of the uterus in a position beyond that of normal is called anteversion. The causes are shrinking of the broad ligament following chronic inflammation (the cervix is pulled to the posterior and is kinked sharply against the body), shortening of the rectouterine ligaments, or rarer, scars and adhesions which pull the uterus forward. In uteri with poor musculature there is a tendency to anteflexion. In retroversion, the uterus occupies a posterior position and is fixed. Temporary retroversion is seen when the bladder is overfilled. The physiological bend is gradually lost and the uterus becomes straight. From a retroversion, a retroflexion may develop when the uterus is soft, flexible and lifted and kinked far beyond its normal range of motion; the body falls backward toward Douglas' cul de sac, the under surface points upward, and makes a sharp angle open to the posterior with the cervix. If the condition persists for a longer time, the uterus becomes thick and hard from passive congestion in the veins of the broad ligament. The causes are: relaxation of the retrouterine ligament, the cervix sinks forward and downward; shrinking of the round ligament which pulls the cervix forward and fixes it there, while the body sinks posteriorly; shrinking processes which pull the uterus posteriorly or to the front. Retroflexion, moreover, may also be caused by developmental failure; Hunter's ligaments (ovarian and round ligaments) allow the ovaries as well as the fundus to be pulled backward and upward and do not pull the uterus into the normal anteversioflexion position (Kustner).

Prolapse of the Vagina and of the Uterus.—The uterus may gradually slide downward from the pelvis, the cervix becomes visible at the vulva; finally a part of the uterus, (incomplete prolapse), or perhaps the entire organ (complete prolapse), lies outside of the external genitalia and is covered by the vagina turned inside out. The tissues in the prolapsed part become hypertrophic; their surface, since it is no longer moistened by uterine mucus, becomes horny, dry, and often brown as the outer skin. External insults lead to defects in the epithelium and actual ulcers (erosive ulcers, abrasions, decubitus ulcers), particularly on the lower part of the prolapsus, *i.e.*, in the region of the cervix, but they may also appear in the vagina, etc. According to Kermauner, these are tear or rupture ulcers. As a rule the os is lacerated, as favored by old cervical tears, and the mucosa becomes more and more everted (ectropion). Both lips may be so completely everted that the region of the internal os becomes the lowest part of the prolapsus (J. Veit). The everted part of the mucosa may be covered by squamous epithelium, while the glands undergo atrophy; erosions also appear (see p. 1635). The prolapse is either replaceable or its reposition into the pelvis is prevented by adhesions. Cystocele (see p. 1446), is quite common. In well marked cystocele, the urinary bladder slips downward; the urethra is usually pulled down along with the prolapse. But it is only in very marked prolapse that diverticuli are developed from the anterior lower wall of the rectum (rectocele).

But not every tumor seen with the vagina turned inside out is a prolapse even though protruding from the vulva with the os uteri visible; in many of these cases which look like prolapsus (see fig. 822), the os is actually in front of the vulva, but the fundus is almost at its normal height; the uterus, usually, but not always, is retroverted. The uterus is therefore enormously elongated; it may reach 12 or 15 cm. in length.

According to Schroeder, the condition is primary prolapse of the vagina involving only the anterior, but perhaps also the posterior walls. The vagina, torn and relaxed from childbirth, sinks downward and pulls on the cervix which responds to this stimulation by hypertrophy. The three parts of the cervix (p. 1643) react in this hypertrophy in varying ways. If only the anterior vaginal wall is prolapsed, the hypertrophy involves the middle of the cervix; if both the anterior and posterior vaginal walls are prolapsed, the supra vaginal portion becomes thickened and elongated, in which case the vaginal portion also is very markedly thickened. The fundus of the uterus may or may not prolapse, because it might be kept in its normal position or be fixed by pathological condi-

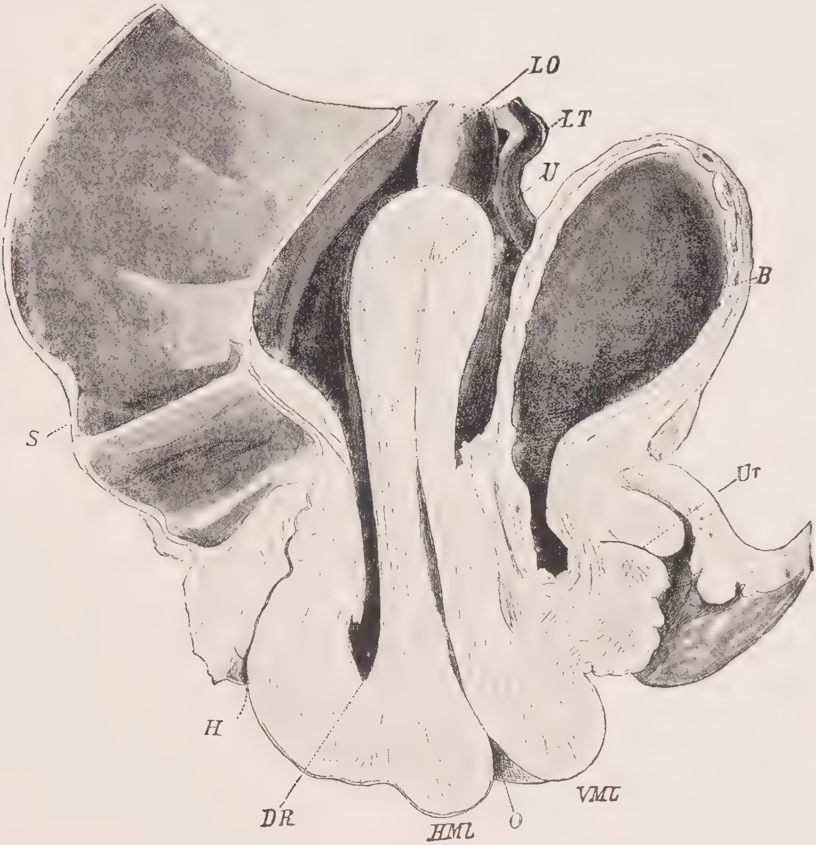


FIG. 822.—Almost median section through a prolapsus of vagina, chiefly its anterior wall with sinking of the 12 cm. long uterus (U). Hypertrophy of portio media cervicis; VML, anterior lip of os fuses with the thickened everted anterior vaginal wall; HML, posterior lip; O, ext. os uteri projects at vulva; H, posterior vaginal vault preserved, bounded anteriorly by the everted part of the posterior vaginal wall which blends with HML; Ur, urethra cut in front; B, bladder with cystocele; Rectum (sectioned outward from midline) separated from the sigmoid S, by a rectal valve of Houston; LO, l. ovary; LT, l. tube; DR, lowest point of Douglas' space; ⅔ nat. size.

tions such as adhesions and tumors. The os uteri follows the vagina as it is gradually pulled in front of the vulva. The prolapsed vagina is thickened. If, however, conditions arise which jeopardize the security of the fundus at its old height, *i.e.*, conditions such as relaxation of the ligaments after childbirth or increased weight of the organ and increased pressure, or if the previously hypertrophic uterus undergoes atrophy following senile involution, or after long continued retention of a pessary, then, to prolapse of the vagina, there is added that of the uterus, with final complete prolapse of both organs. In other cases, the prolapse is a primary falling of the uterus with secondary inversion of the vagina. This occurs particularly easily when the normal position of the uterus is changed, as in retroversion or retroflexion, because the abdominal pressure exerted normally on the upper wall of the uterus tends to keep it in anteversion, but is now exerted on the fundus or even on the lower wall of the uterus, and thus forces the organ more and more into the position of retroversion, *i.e.*, out of the pelvis (Kustner). The uterus as it sinks pulls the vagina after it. For the same reason, retroversion or retroflexion is usually accompanied by some degree of descensus. Total prolapse may develop quite quickly, especially when the pressure is increased, *e.g.*, by carrying or lifting; the uterus need not be particularly heavy or particularly large, but when it is, the prolapse is favored. If the prolapse is of gradual development, both the uterus and the cervix may be hypertrophic from venous stasis, from torsion of the ligaments, or from binding by the vulva; in part, it is due to temporary edema, and in part, to true fibrous tissue hyperplasia, a good example of hyperplasia following venous hyperemia and chronic edema. If the tissues fixing the uterus are loose, if the pelvic tissue is relaxed from loss of fat, if the uterus is large and heavy, or if the uterus in the vagina is overstretched from a large pessary for instance, a complete prolapse may occur suddenly or gradually, either at one increase or recurring increases of intraabdominal pressure. Halban and Tandler have placed the greatest responsibility on the normal and disturbed function of the pelvic musculature. The most important factor in this connection is the pelvic diaphragm, made up of the levator ani muscle through which the rectum passes posteriorly and the vagina and urethra anteriorly (hiatus genitalis), and on which the upper portion of the posterior wall of the vagina and the cervix rests; the anterior wall of the vagina from the posterior part of the floor of the bladder above the interureteral plica lies upon the hiatus. If the hiatus is dilated or if the fibers of the levator, especially those which surround the hiatus, are torn, *e.g.*, during childbirth, the conditions for prolapse are thus fulfilled, and the first portions to fall are those parts of the vagina and the bladder which lie over the hiatus. Usually at first, only the cervix, and later the uterus, pass through the hiatus. If the upper part of the uterus remains thick and fixed on fibers of the levator, the lower part is pulled out and thickened. These views are held by Kronig and v. Jaschke, among others. The occurrence of prolapse in occult spina bifida (see under this subject) and the prolapse in the newborn in sacral spina bifida (Graf), are used as proof for the great importance of the muscle apparatus, (levator ani). If the fourth sacral nerve, the motor nerve of the levator ani is involved by the spina bifida, the muscle undergoes degeneration and prolapse follows; the fibrous ligamentary apparatus is however unchanged. On the other hand, Martin (lit.) emphasizes the connective tissue bands and fascia as paramount in supporting the female genital organs. Sippel shares this opinion. See, among others, the critique of Schulz concerning these statements; v. Franque is of the opinion that in spite of the recently acquired anatomic knowledge of the suspensory apparatus of the internal genitalia which has led to changes of opinion, in the future we will still believe that the conception of Schroeder is the most important.

Inversion of the uterus is, at first, an inversion of the fundus into the body (first stage); in complete inversion (second stage), the fundus is projected through the os, and finally the inverted uterus is prolapsed (third stage). Viewed from inside the abdominal cavity, the condition is recognized as a pocket book-like cavity in which the tubes and ovaries are lying. The causes: first, acute inversion takes place during childbirth or in the puerperium, spontaneously, or, *e.g.*, from pulling on the umbilical cord and the placenta. Usually, according to Schroeder, it is gradual when tumors with broad bases are situated in the fundus and produce atrophy of the uterine tissue where they are attached. This produces a soft place in the firm uterine tissue which sinks inward; the tumor pulls it downward with the help of contractions of the uterus. Vigorous contractions hasten this occurrence.

Stenoses and Atresias of the Genital Canal and Their Consequences. Rupture and Tears of the Uterus.—Stenoses and atresias of the genital canal (gynatresias) are congenital, (see p. 1475), or acquired as a result of inflammatory swellings of the os, of ulcerating cicatricizing changes, *e.g.*, gangrenous vaginitis in the infectious diseases (diphtheria), of childbirth, of trauma with subsequent scars following tears or ulcerations, of amputation of the os or also of tumors, etc. In total atresia, *i.e.*, obliteration, there is no lumen at all. Senile obliteration is common at the external or internal os or in certain favored situations in the body. These occur by the growing together of adjacent parts after loss of epithelium. As a rule, these adhesions give no symptoms and usually there is a mild hydro- or pyo-metrium (see below).

Gynatresias become important with the onset of menstruation since they cause an accumulation of blood and dilatation above the obstruction. When the vagina is closed by the hymen (atresia vaginae hymenalis), the vagina is distended with blood (haematocolpos). The blood is like tea or chocolate, or is black and much thickened. Later the uterus, but first the cervix, is overstretched. When the vaginal atresia is higher, the cervix is soon stretched and later the body of the uterus also (haematometra). When the external os is closed, the entire organ may reach the size of a man's head; the walls may be thick, or as thin as paper. When the internal os is obstructed, the contour of the cervix remains unchanged, but the body of the uterus is stretched out in globular fashion. The tubes may also be dilated and become blood-containing sacs (hematosalpinx); this occurs less frequently from back flow of blood from the uterus, since the interstitial parts of the tubes are very narrow, than from autochthonous (menstrual?) bleeding into the tube when the abdominal opening is closed; if the latter is open the blood flows into the abdomen. If the external os is obstructed after the menopause, the fluid is serous or mucoid (hydrometra). The dilatation is usually without significance and always less than in hematometria. Occasionally the uterus with atresia is somewhat dilated and filled with a cloudy white glistening mass (cholesteatoma of the uterus, see pp. 1625 and 1419). In pyometra there is a suppurative catarrh. A particular kind of pyometria with very little dilatation often occurs in the atrophic thin-walled uterus of older women from the collection of a slimy purulent fluid behind the atresia of the internal os (pyometra senilis). If the purulent or bloody-purulent contents undergo decomposition, there arise gases, and the uterus is stretched into a hemispherical form (physometra, very rare). Physometra (tympania uteri) may also occur from the entrance of air into the uterus during childbirth, or following the production of gas from gas-forming bacteria. See under diseases of the puerperium.

Consequences of hemato-, pyo-, and physometra; rupture of the obstructed part follows necrotic or gangrenous inflammation, *e.g.*, in hymen atresia, or following trauma. The contents enter the abdominal cavity or the parametrial tissues or perhaps the bladder, the rectum or even to the outer surface. Even a hematosalpinx may rupture from trauma; a profuse hemorrhage with peritonitis, or a hematocele may result. In reduplication of the genital canal and unilateral gynetresia, hematometria and hematocolpos develop unilaterally; a hematosalpinx may also be present.

Ruptures and Tears of the Uterus.—Occasionally, spontaneous rupture occurs in the parturient uterus; the site is practically always at the cervix, and is the most serious injury which may occur to these parts. The over-stretched vagina may initiate the process, or it may follow compression. The causes are usually difficult labor, disproportionate sizes of child and pelvis, particularly in contracted pelvis, transverse position, hydrocephalus, local changes in the wall of the uterus, particularly in multiparas (changes in the elastic tissue, see O. Horn,) older scars, the scars of Cesarean sections (see Baisch), deeply imbedded placentas, as in placenta accreta in which, as the author has observed, there is a striking thinness of the uterus (see Futh). Adenomyometritis may also be the cause of ruptures during pregnancy (Volk, Mayer, Schafer, lit.). The situation and shape of the tears are variable; in a narrow pelvis they are oblique and high, in an obliquely lying pelvis they are lateral; compression on the promontory results in rounded tears. Other ruptures occurring during childbirth, which, with v. Winckel, are classified as violent, may occur from instruments, forceps, etc. Occasionally a spontaneous rupture just begun is completed by very mild manipulation such as introduction of the hand. Ruptures in uterine diverticuli as a result of pregnancies (Schickele, Barchet, Piskacek, lit.) or septic infections (Hellendall) are very rare.

Hematometra may also, as stated, lead to rupture. Bauereisen saw rupture of a cervix full of telangiectases (Falk). Tumors such as myomas, sarcomas and carcinomas in the substance of the uterus may lead to rupture during pregnancy, or to ordinary ruptures, usually in the body. The deep lateral cervical tears from rapid progress of the child, and which involve the neck and often the point of attachment of the vagina are important, since they open the parametric cellular tissue. Severe, even fatal, hemorrhages may occur, or an intraligamentary hematoma may be developed, (uterine artery), or there follows a puerperal wound infection. Deformities may result. Superficial tears in the cervix during childbirth are very common.

Circulatory Disturbances and Hemorrhages of the Uterus. The Endometrium.—Anatomy: the cavity of the uterus is lined by a mucous membrane attached internally to the muscle and covered externally with a single layer of ciliated cylindrical epithelial cells; (according to Mandl not all places are covered with ciliated cells); the movement of the cilia is from within outward, (Hofmeier). There are many tubular glands also lined with ciliated epithelium. The surface and the glandular epithelial cells are bordered on the outside by a membrana propria (membranous thickening of collagenous fibers, Hormann). The interglandular tissue is soft and composed of rounded or oval cells poor in protoplasm which lie in a fibrillar connective tissue network very difficult to see; the cell body and the boundaries are also usually difficult to define in microscopic sections. The nucleus dominates; the size of the cell is about that of a white blood cell. In childhood the endometrium contains rounded and later spindle shaped cells. According to Hormann, there are both an intercellular scaffolding and a network of fibers consisting of prolongations from the cells. Since the glands are placed in the mucosa both in vertical and oblique directions, and since here and there one or another of the glands enter the muscularis for a slight distance, in every section the gland lumena are cut transversely or obliquely or even longitudinally. The glands secrete a thin mucus, sterile under normal conditions. For the lymph vessels, see Kroemer, v. Franque. In the lower two-thirds of the cervical canal, the glands are of the acinous branched form; in the upper third they are cylindrical, but shorter than those in the uterus. The cervical glands secrete a glassy, thick mucus, free of bacteria and strongly bactericidal. Numerous folds make the secretory surface of the cervix very large, and more secretion is produced here than in the uterus. The cylindrical epithelium of the cervical canal is higher than that of the uterine canal; in the latter the nuclei are in the middle of the cell; in the former they are situated at the base. See Wegelin concerning glycogen in the epithelial and stroma cells.

Active hyperemia of the uterus is found in inflammation, and physiologically during menstruation.

In contrast to its ordinary pale appearance, the endometrium of the body during menstruation is reddened, softened, swollen, damp, and covered with dark blood. The mucosa of the cervix is pale. Even the wall of the uterus is softer and juicier than normal. Actually, the entire internal genitalia are hyperemic, but a true menstruation of the tube, perhaps, does not actually occur (Czyzewicz).

Occurrences during Menstruation and Its Disturbances.—A complete description is given by Schroder (lit.).

Menstruation occurs at regular intervals of 3¼ to 4 weeks. The amount of blood lost by a normal youthful individual is about 37 cubic centimeters (Hoppe-Seyler); the reason menstrual blood does not coagulate is not known, but see Birnbaum and Osten, Haslinger, Stickel and Zondek; according to Kristea and Denk, Cantoni, there are no peculiarities in menstrual blood in regard to its coagulative abilities. See Schick concerning "menstrual poisoning." The beginning of menstruation, in our climate, occurs from the twelfth to the fifteenth year of age, the menopause at about the forty-fifth to the fiftieth year. The importance of menstruation is in its preparation of the mucosa of the uterus to receive an impregnated ovum (Jossel-Waldeyer, Hitschmann and Adler). According to Schroder, menstruation does not serve a purpose in itself, but is a part of the cycle for the preparation of pregnancy.

There are many opinions concerning the condition of the corpus luteum or the relation of the corpus luteum to menstruation. These have been mentioned on p. 1544. Seitz and Wintz postulate a very close relationship; stages in the function of the corpus luteum (see p. 1544) are related to phases in the menstrual cycle: 1—ripening and stretching of the follicles leads to premenstrual changes in the mucosa; 2—the stage of proliferation brings the premenstrual preparations to their full development and leads to the secretory phase in the endometrium; 3—the blossoming of the corpus luteum holds back the secretory phase in the endometrium and through its hormone stops the beginning of menstruation; 4—during the regressive phase of the corpus luteum, the inhibiting influences disappear and menstrual bleeding takes place. According to this, the corpus luteum therefore hinders menstruation. In pregnancy, the corpus luteum is at first persistent; there is, therefore, no menstruation; further along in pregnancy, the placenta is said to take over the function of the gradually disappearing corpus luteum as a gland of internal secretion, (see Halban and p. 1543). Labhardt doubts that these structures are the cause of bleeding, because the luteolipoid of Seitz has no specific influence on menstrual bleeding. Schroder also believes the bleeding is purely a uterine process.

The Occurrences in the Uterine Mucosa.—The mucosa of the uterus, *i.e.*, of the body (very little in the cervix), swells during the premenstrual phase, *i.e.*, about ten days before menstruation (Leopold); the otherwise scarcely visible capillaries are double, or even four times their normal size (stage of proliferation); the mucosa is divided as a decidua into three layers, a superficial compact, a deeper, spongy (both together are the functional layers, Schroder), and a basal layer which contains the fundi of the glands, and which remains unchanged. The epithelial cells of the glands become larger, longer and thinner; the glands in the spongiosa dilate, and become like cork-screws; they derive branches, which appear like papillary growths in the wall, and are filled with much mucoid secretion of the epithelial cells. The connective tissue in the compacta which contains the gland ducts is swollen, its cells more rich in protoplasm and like decidual cells, (see H. Albrecht), the nucleus becomes less stainable. (Lofquist and Essen-Moller believe this decidua-like formation is always pathological.) The epithelial and stroma cells and often the lumena of the glands contain many glycogen (see Wegelin, lit.) and fat globules (Aschheim, Sugi). There are also rich collections of round cells, usually near to the musculature (Hitschmann-Adler for details and lit., see also Hartje, Iwase). It is assumed that the accumulation of glycogen during the premenstrual swelling of the mucosa is a sort of preparation for the taking up of the ovum (Schroder speaks of the phase of secretion). According to the older views, which, however, are still believed by Meyer-Ruegg, blood leaves the vessels by diapedesis and by rhexis during the stage of highest congestion; this infiltrates the interstitial tissue, forces its way between the epithelial cells into the glands, lifts the surface epithelium in places and reaches the lumen of the uterus to be expelled intermittently by contractions of the uterus. This function is performed only by the surface layers of the mucosa (von Kahlden, Hitschmann and Adler) (desquamation-stage, *i.e.*, true anatomic menstruation), but according to the observations of Schroder and others, it is a function of $4/5$ of the endometrium which finds itself in the stage of menstruation; the layers gradually break up, beginning above, or come off, usually in small fragments. According to Schroder, bleeding then takes place from the blood vessels in the remaining basal layer which now shows a torn surface. According to Meyer-Ruegg, the remaining mucosa, after expulsion of parts, looks about like the mucosa after an abortion. When the hemorrhage has ceased there is expelled a lighter, scantier, more viscid, cloudy secretion which soon ceases entirely, and this marks the beginning of the stage of regeneration. In four days the basal layers are covered by epithelium, and in six to ten days another functional layer has grown three to four times as thick as the basal layer; this then enters the stage of proliferation. This stage is also spoken of as the interval or the post-menstrual time. The epithelial cells begin to show signs of secretion only in from fifteen to sixteen days after their further growth has stopped; this increases to the end of the cycle (secretion phase). Schroder recommends the terms "premenstrual," "proliferation stage" (four to fifteen days), "secretion stage" (fifteen to twenty days), "desquamation and regeneration stage." Ordinary menstrual bleeding (normal three to four days) may be increased both in time and amount by constitutional diseases such as chlorosis and anemia, and by local disturbances such as changes in position, inflammations, tumors, etc., (menorrhagia).

Bleeding from the genitals of newborn infants is called menstruatio precox; it is the result of venous stasis or infectious processes (see Zappert). Verebely saw precocious puberty in a six year old girl with an ovarian sarcoma; after removal of the tumor the infantile stage returned (see also under pineal gland).

Membranous dysmenorrhea is a colicy or painful condition characterized by the expulsion of tags or membranes with the menstrual blood. The structure of these masses, which are of considerable practical importance, may vary considerably: (*a*) most of them are exfoliations of parts of the uterine mucosa (exfoliative endometritis or menstrual decidua). Under certain circumstances, a three layered cast of the entire uterus may be expelled; it is raw, and villous on the outer surface, and smooth on the inner surface with indentations corresponding to the uterine glands. Microscopically, the membranes are composed of uterine mucosa, but the findings vary, according to the menstrual stage at the time the cast is formed. Usually the mucosa is diseased, is thick and soft and infiltrated by leucocytes, so that during menstruation, larger and thicker particles may be loosened. There are thus found microscopic networks and tags of fibrin, red and white blood cells, and tags of mucosa with uterine glands containing changed or unchanged high epithelial cells, a large number of round cells somewhat resembling young deciduae cells, along with a rich reticulum showing focal hemorrhages and fatty degeneration. Hitschmann and Adler (lit.) believe the condition for the loosening of these discharges lies in the peculiar laminated structure of the menstrual mucosa, which consists of a compact part and an edematous spongy part from which the former may be separated when the internal os is obstructed, and the contractions of the uterus are thus more vigorous (see also Meyer-Ruegg). According to Lindner, it is only an extensive physiological degree of desquamation of the mucosa; Hitschmann and Adler do not believe there is an inflammatory cause behind it; the leucocytes contained in the membrane have wandered in at the beginning of menstruation and were not there before; thus they are only a part of the menstrual picture. (*b*) These membranes may come from one or more situations covered by squamous epithelium; in isolated cases they show small holes representing the lumena of glands which are surrounded by flat, concentrically arranged epithelial cells in several layers. But such membranes, if they consist only of squamous epithelium, come from the vagina or from the external os. (*c*) They may be composed of fibrin, red, and many white blood cells, *i.e.*, products of coagulation. They do, however, give the impression of true tissue membranes. It is assumed that the membranes remain in the uterus from the previous menstruation and thus become thickened. (*d*) Occasionally, the expelled masses are muco-fibrinous or almost pure fibrin, are solid or "cystic" with smooth external and uneven internal surfaces, appearances which need not have inflammation present to bring them about, (exfoliation of the mucosa or fibrinous exfoliation). A familial hereditary tendency has been observed (lit. Meyer, Lohlein). In a 59 year old woman with a myoma of the uterus, who had not menstruated for seven years, Wallart saw repeated expulsions of polypoid fibrin coagula covered by squamous epithelium (plastic fibrinorrhea).

Occasionally a previous abortion is behind these pseudo-membranous dysmenorrheas. The differentiation between ordinary membranes and parts of placenta, a differentiation of great practical importance, depends microscopically upon the demonstration of the characteristic chorionic villi (fig. 871). It is often difficult to decide from a small piece of tissue spontaneously ejected from the uterus, perhaps as a three cornered sack, whether it is menstrual deciduae or the decidua of the first few weeks of a pregnancy, extra- or intrauterine, which has been expelled. As stated, the cells in the interstitial tissue of a menstrual decidua occasionally become larger (p. 1620), similar to those in the pregnant decidua, although the cell bodies of the latter are especially enlarged and appear like squamous epithelium, in groups and broad sheets; but even these differential points are not always reliable (see Eicke, lit.). The blood vessels are much more dilated than in the menstrual decidua. More important than these changes, however, is the fact that the epithelial cells of the surface and those in the glands are not changed in the menstrual decidua; they are high and cylindrical, whereas in the pregnant decidua they are low, cuboidal or flat, like endothelial cells. In very early pregnancy these criteria may not be present; in this case if a sac is expelled it is necessary to hunt for the ovum. (See the observations of Hitschmann; more details under decidua, p. 1709.)

Metrorrhagia may also occur in the hemorrhagic diatheses, during the course of various infectious diseases such as cholera, typhoid fever, small pox, and in intoxications with phosphorus, in inflammations and especially in tumors such as myomas, carcinomas, and mucosal polyps. These are atypical hemorrhages, since they occur irrespective of the times of the menses, pregnancy and the puerperium.

In the uterus are solid masses of blood which extend long outrunners into the tubes. These masses may be expelled, only to be renewed.

In the very aged, hemorrhages into the mucosa which usually do not reach the cavity of the uterus are very frequent and have been called uterine apoplexies by Cruveilhier. They are said to be due to nutritional disturbances, especially those secondary to sclerosis and calcification of the uterine arteries (v. Kahlden, Simmonds, Kon and Karaki). They may have clinical importance, the hemorrhage being severe enough to justify extirpation of the uterus. It has also been pointed out that sclerosis of the arteries where the placenta is attached may lead to fatal postpartum bleeding (Kustner). It might be mentioned that these arteries become affected very early; perhaps they are the first of all the arteries in the body to show sclerosis (see p. 106). In a large group of pathological uterine hemorrhages, the cause may be resident in diseased arteries, in an endometritis, or, perhaps, more often, in a disturbed ovarian function (see p. 1630), which, according to the opinion of many authors, is responsible for the severe hemorrhages often seen in hyperplasia of the uterine mucous membrane (see p. 1626). According to Theilhaber (lit.) and his pupils, these bleedings are due fundamentally to an abnormal condition, not only in the anatomy of the uterine musculature, but also in its functional capacity, thus to atony, but most of these hypotheses have not been verified by actual findings (see Schickele and Keller, lit.).

Passive congestion is found in various malpositions of the uterus, (see p. 1611), and particularly in heart failure. The uterus is enlarged, tough, blue gray; the mucosa is traversed by wide veins; it is dark red, swollen, moist, and infiltrated by small hemorrhages.

Occasionally phlebectasias are seen in a uterus of normal size, but they may reach such importance that the entire wall appears to be cavernous; when the blood vessels are empty the surface becomes pitted; in the venous plexuses (ovarian and utero-vesical) veins as thick as thumbs may be seen. Such a general phlebectasia in the uterus may occur during pregnancy similar to the varices in the brain (see p. 162), and the varices which lead to thrombosis in the vagina (p. 1699). The author has published a case (see p. 162), in which general phlebectasia led to atony of the uterus immediately after childbirth and to death from hemorrhage.

Among the hemorrhages into the peritoneal cavity in the neighborhood of the uterus, the most important, the retrouterine hematocele, has been discussed under tubal pregnancy (p. 1608). Hematomas of the broad ligaments have also been mentioned (p. 1608); hematomas may arise in this situation from rupture of a varix. Hemorrhages into the retroperitoneal cellular tissue and infiltrating perhaps into the actual peritoneum, may also be caused by squeezing of the uterus during childbirth or following rupture.

Inflammations of the Uterus and Its Vicinity, Not Including Puerperal Infection.—The intimate relationship of the constituents of the uterine wall is expressed by the fact that inflammations are rarely limited to one part. Thus in inflammations of the mucosa (endometritis) there is usually an inflammation of the bordering layers of the intermuscular connective tissue (metritis); on the other hand, in a metritis there is often an accompanying inflammation of the endometrium and of the peritoneum which is tightly adherent to the musculature; the inflammation of the peritoneum is called perimetritis. Nevertheless for practical purposes, it is wise to name the parts in which the disease is most manifest.

Inflammations of the Uterine Mucosa: Endometritis. Acute Endometritis.—The mucous membrane is swollen, hyperemic, softer than normal, is infiltrated by cells and may show punctate hemorrhages. Occasionally the changes are limited to the body or to the cervix. The secretion is increased in amount; that from the cervix is muco-purulent; that from the body is thinner. The cervix produces more secretion than the body (see p. 1618). The microscopic picture is characterized by hyperemia, exudation of a serous fibrin-containing, leucocytic fluid into the interstitial tissue, and leucocytes in the lumena of the glands and on the surface. (For the histology of gonorrheal inflammations, see p. 1593.)

Etiology.—Acute endometritis may occur during menstruation, in the puerperium, following intrauterine medication, and uncommonly, from inflammation in the vagina through dirty tampons, pessaries, etc. It is often gonorrheal, and usually remains localized in the cervix, although, according to Wertheim, gonorrhea may progress beyond the internal os; he, furthermore, states that the ordinary findings in gonorrhea of the uterus are suppurative catarrh and interstitial endometritis, usually with an increase in the number of the glands. But, as a rule, the connective tissue between the upper layers of muscle is also involved; *i.e.*, there is a metritis also. Occasionally, a hemorrhagic endometritis of the body which leads to cellular infiltration, exudation into the tissues and atypical bleeding, occurs during the course of the acute infectious diseases such as cholera, pneumonia, typhoid fever, scarlet fever and others.

An "ammonia excretion" endometritis occurs in uremia from excretion of urinary substances, particularly decomposition products of an ammoniacal nature (Schlagenhaufer), but this is an uncommon condition.

Chronic Endometritis.—This is very much more common than acute endometritis, and may involve the entire uterus, the body or the cervix. It occurs in various forms and was formerly considered the chief representative of diseases of women.

Later investigations, particularly those of Hitschmann and Adler, led to a revision of this teaching of chronic endometritis, a revision which has been very fruitful. This will be discussed on p. 1628 and following.

Chronic endometritis may be a chronic catarrh with hypersecretion, usually involving both the body and cervix and seen frequently in chlorotic girls and sterile women. It also follows abortion, normal childbirth and myomas. A chronic hemorrhagic "endometritis" is a common finding; in heart failure it is characterized by swelling, venous hyperemia and hemorrhages. The hemorrhages, the causes of which are probably not only in the endometrium, (see p. 1631), leave behind a gray pigmentation. A chronic gonorrheal endometritis is often a chronic interstitial inflammation; it may spread to the tubes and the perimetrium, and is a frequent and characteristic finding in prostitutes. The tubes are either stretched and greatly thickened, being as long and as thick as fingers and filled with pus, or are much convoluted with the ends adhering and with many adhesions occurring between the adnexa, the uterus and the rectum. In atrophic endometritis, the glands disappear along with the epithelium, and the mucous membrane shrinks to a thin covering; the round cells become spindle shaped; later the lining of the uterus consists of fibrillar tissue. The surface is spotted gray or brown and remains of glands may dilate to small cysts (chronic cystic endometritis). Atrophic endometritis may be an end result or shrinking stage of such forms of hyperplastic endometritis in which the connective tissue grows particularly rapidly, forms spindle-shaped cells in the stroma which choke off the normal tissue, and becomes infiltrated with lymphocytes (chronic interstitial endometritis, C. Ruge); shrinking of the previously thickened tissue causes atrophy and choking off of the glands with occasional obstruction and cystic dilatation of these structures. But atrophic endometritis may also be a senile change; if atresia is developed in the uterus, the cavity becomes filled with a muco-purulent fluid (pyometria senilis). The wall is much thinned, shows senile involution, and is overstretched.

Metaplasia of the Epithelium.—Replacement of the cylindrical epithelium of the uterus in chronic endometritis by layers of squamous epithelium which may cornify, is so uncommon, contrary to the statement of Zeller, that with Hitschmann, we must deny its occurrence under these circumstances. When, however, such an epidermoid appearance does occur in the uterus (Veit), especially in old age, it is always important to investigate and see if it is not carcinomatous. There do occur cases, however, in which squamous epithelial cells are found in places among the cylindrical epithelium (compare the author's communication in C. f. Schw. 7, 1906), particularly on the surface of the mucosa or in the depths of the glands. It must be remembered, that, without further investigation, it is not correct to consider this a metaplasia, since islands of squamous epithelial cells can be found under normal conditions, and even in children (see Friedlander, R. Meyer). Hunziker saw islands of squamous epithelial cells in currettings from the body of the uterus and believes they are maldevelopments of the tissues; on the other hand, upward growths are known to take place from the os or the cervix into the uterine cavity (see Ruge). If the dilated thin-walled cavity is filled with a glittering pulp of atheromatous material made up of cholesterin and masses of squamous epithelium, and if the mucosa has been thinned to a few remnants of glands and is covered with cornifying layers of squamous epithelium, the condition may be spoken of as cholesteatoma of the uterus. These cases are close to the boundary line of surface carcinomas (see p. 1688). Epithelial metaplasia often occurs in polyps also; it appears usually by pushing away the cylindrical epithelium, or shoving itself underneath and lifting the epithelium off, or it arises from indifferent cells in loco. It can further be mentioned that the uterine epithelium of adults may consist of several layers (2–3) without metaplasia, as the author pointed out in earlier editions of this book. Many layers, likewise without metaplasia, are, on the other hand, quite rare (Hengge), and are important because of differentiation from carcinoma; the uniformity of the many layers gives the clue. The author has seen such conditions in curettings.

Occasionally several layers of atypical squamous epithelial cells are found at the os and in the internal surface of the cervix, which may be distinguished from typical squamous cells by their size, the chromatin content of their nuclei, and their less regular architecture; these layers have a tendency to spread into the glands in the form of narrow or wider cloaks, and thus replace the original cells. Many authors believe this change is distinctly malignant. The differentiation is often difficult (Schauenstein); the author has called attention to similar epithelial changes in polyps (see p. 1634, Philips).

Hyperplasia of the Uterine Mucosa and Its Relationship to Chronic Endometritis.—**Hyperplasia of the uterine mucosa,** a condition frequently seen in curettings, was formerly called chronic hyperplastic endometritis (fungoid, Olshausen), and considered the expression of an inflammatory hemorrhagic condition of the endometrium (see p. 1630). The curettings of such cases show large masses of mucosa in which the glands are quite numerous, but in which the stroma is always more or less changed. The mucosa is pale or whitish red and reaches several millimeters in thickness, or even 1 to 2 centimeters; it is a soft relaxed, easily torn, loosely attached, or porous lining, often filled with light translucent bubbles (dilated glands). Since the hyperplasia is not uniform, but is more marked in some places, the internal surface of the uterus becomes speckled, wavy, villous or polypoid.

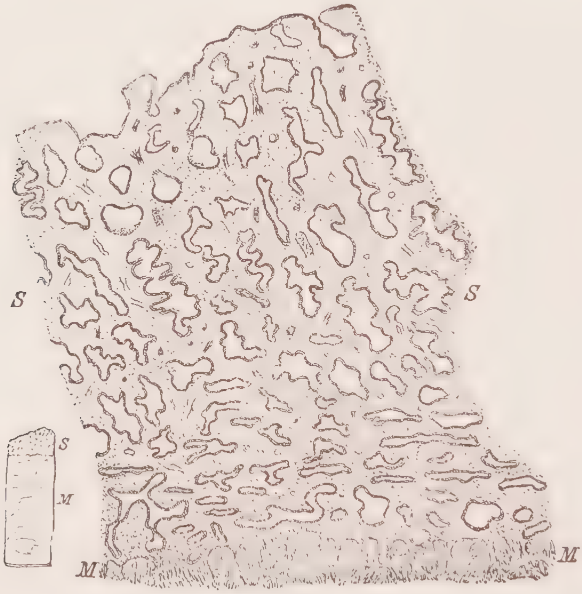


FIG. 823.—Hyperplasia of endometrium; S, thickened mucosa in which polymorphous glands lie in cellular interglandular tissue; M, musculature; (low power). The small illustr. shows in ¾ nat. size the comparative thickness of the mucosa to the whole wall.

The condition has nothing whatever to do with the independent polyps which arise from the basal parts of the endometrium (see p. 1632).

The descriptions given by the older authors of so-called hyperplastic endometritis are particularly concerned with (*a*) changes in the glands, and (*b*) changes in the stroma.

(*a*) The hyperplasia of the gland cells, which often show many mitoses, does not cause a piling up of the number of cells, but rather, an enlargement of the surface of the glands which later leads to dilatation. enlargement, and finally to tortuosity of their tubes with outgrowths and branching buds jutting into the lumena, whereby on cross section, cork-screw and saw-tooth-like forms are found. In profile, the epithelium growing into the lumen looks like papillae; they are, however, only comb-like outgrowths similar to the picture seen in transverse section of a tube, where the folds also look like pseudo-papillae. But in addition to this growth in the direction of the lumen (inverted growth, Gebhard), pictures also occur which have been called invagination; on cross section two or even three glandular rings are found placed one in another. But most of these pictures which have been considered by Gebhard as true ingrowths (form of inverted growth) are artefacts; they are either loosened glands from the lower layers, cross sections of convoluted glands, or papillary ingrowths. Everted growths were described by Gebhard as grape-like forms, which arise from new glandular branchings. The hyperplastic glands grow closer together (normally a field contains perhaps four or five cross sections of glands). The contents of the glands are mucus, sometimes mixed with desquamated epithelial cells, leucocytes and blood. Occasionally many glands become cystic from obstruction of their ducts.

(*b*) The stroma is saturated with serum, is rich in blood, and the capillaries are dilated. The interglandular tissue is infiltrated by small cells; its cells grow, take on spindle shapes or epithelioid decidual forms without however, as a rule, assuming the close relationship of true large decidua cells. If the growth of the interstitial tissue is dominant, an interstitial endometritis will result, (C. Ruge), and the glands, particularly in their lower parts, are pushed far apart from each other, while the spindle-shaped cells are commonly distributed in focal situations; this form of inflammation which, in its chronic condition, is chiefly due to gonorrhea, may lead to final atrophy of the mucosa (see p. 1624).

On the basis of microscopic findings, the opinion was expressed that this so-called hyperplastic endometritis was an inflammatory process. In one case both the glands and the interstitial tissue are equally affected (simple hyperplastic endometritis), while in another case, either the growth of the glands (hyperplastic glandular endometritis) or of the connective tissue (interstitial endometritis) is dominant. In later years, however, especially after more knowledge was accumulated in relation to the changes during the menstrual cycle, there has been a complete reversal of opinion in regard to hyperplastic endometritis.

The investigations of Hitschmann and Adler (Hartje, Theilhaber and Meier and others) have been particularly valuable in showing that the pictures in inflammatory hyperplasias are often only the normal endometrium in the stages of the menstrual cycle, (see p. 1618), *i.e.*, a hyperplasia of the glands which has nothing to do with inflammation. No doubt many cases with normal endometrium have formerly been called glandular endometritis since no account was taken of menstrual changes. Even in the diagnosis of interstitial endometritis, the same skepticism must be shown (Hitschmann and Adler); in this condition the premenstrual changes, particularly the separation of the mucosa into a compact and a spongy part (see p. 1619), may simulate an endometritis. The only real criterion for the diagnosis of interstitial endometritis or endometritis itself, (actually, according to Hitschmann and Adler, there is only an interstitial endometritis), is an infiltration of the connective tissue with round cells and plasma cells which are the best characterized and most constant accompaniment of inflammation anywhere. Spindle cells are, therefore, of no aid in the diagnosis. Other authors, as for example, Weishaupt (lit.), do not agree that the finding of plasma cell infiltrates is of exclusive importance; Weishaupt occasionally found increase in the number of glands along with interstitial inflammatory changes as a part of the post menstrual changes, and this must probably be considered pathological. The author can verify these statements. Theilhaber and Meier (see also Keller, lit.) also do not believe that the finding of plasma cells is the only criterion of inflammation, but that the finding of round cells and pus cells in large numbers is also necessary. Albrecht found plasma cells in only 75% of the cases of chronic endometritis which were otherwise characterized by infiltration of the stroma and changes in the blood vessels, changes which in the great majority of cases are accompanied by secondary proliferation of the glands. For this reason the designation "hyperplastic endometritis with proliferation" is quite correct (see Albrecht and Logothetopulos). Schickele recommends that the term "glandular endometritis" be retained, especially for those conditions secondary in the uterus, *e.g.*, the so-called chronic metro-endometritis, submucus or intramural myomas, carcinomas, inflammations of the adnexa, malpositions, and those conditions due to venous stasis (see p. 1632), even though they have nothing to do with inflammation. Later, however, Schickele and Keller (lit.) themselves recommended that the term "glandular endometritis" be replaced by the terms "hypertrophy and hyperplasia." (See the literature in the appendix.)

According to the views of the author, there are two separate conditions involved, endometritis, the true inflammation, and hyperplasia; this classification incidentally is also useful in the examination of curettings. We ourselves differentiate:

1. **Chronic Endometritis.**—Both the stroma and the vessels show the characteristic changes of inflammation. According to Schroder (lit.), whose investigations the author is prepared to substantiate, there can be differentiated:

I. Mucous membranes with inflammatory changes, but undisturbed menstrual cycles. These consist of infiltrations of round and plasma cells, although the latter are by no means necessary (see Frey); they appear in more or less scattered masses or columns, at one time (*a*) localized as a chronic infection of the basal layers with more or less infiltration or disturbance in the function, at another time (*b*) established subepithelially in the surface, and here leading to ulcerations, or (*c*) diffusely scattered without limitation to any particular layer.

II. Mucous membranes with inflammatory changes in which the cycle of menstruation is disturbed. In these cases, the stroma, the vessels of which are dilated and increased in number, is markedly infiltrated with lymphoid cells, plasma cells and even polymorphonuclear leucocytes. In the lumena of the glands are lymphocytes, leucocytes and desquamated damaged epithelial cells. An accurate correlation with the cycle is not possible.

Albrecht calls attention to the well known deep growth of glandular mucosa into the myometrium, *i.e.*, trespassing beyond the ordinary boundaries, as of particular importance in distinguishing an inflammatory hyperplasia.

2. **Hyperplasias of the mucosa** having nothing to do with inflammation have been described on p. 1626; as stated, the mucosa contains clear vesicles which represent dilated filled glands, and often shows petechial hemorrhages. The uterus is enlarged and tough (women who have borne children). If an attempt is made to determine the menstrual phase from the appearance of the mucosae, the attempt will end in failure for the pathological hyperplasia is not at all similar to any phase of menstruation. The condition often occurs in women after the menopause. The contours of the glands are dissimilar and in parts very irregular; some are straight, some convoluted, some like cork-screws or saw teeth, some are narrow, many are dilated into cysts and filled with mucus which contains desquamated epithelial cells. The epithelium of the gland is high cylindrical and here and there may be present in several layers. The richness of mitotic figures differentiates the glands of the hyperplastic mucosa from those of the hyperplasia of menstruation invaginations (see p. 1627), are seldom

similar to those in fully developed menstruation. Glycogen is also lacking, in contradistinction to the menstrual collection (see p. 1619, Driessen). The glands are more or less close together. The stroma of the hyperplastic mucosa varies in different situations; thick, spindle-celled, relaxed, wide-meshed and translucent edematous parts lie in juxtaposition to each other. Peculiar characteristic masses of blood are also met, (Schroder), and are always present (Driessen); they are probably due to stasis and thrombosis in the thin-walled, markedly dilated blood vessels; they lead to necrotic changes in stroma and glands and to a mild reactive leucocytic infiltration. While the stroma, as a general rule, contains but few cells and shows only isolated lymphocytes or plasma cells, there are cases in which rich focal masses of round cells (lymphocytes and also plasma cells) are found, and which indicate the transformation of an hyperplasia to an inflammation. According to Wegelin, an inflammatory infiltration brings forth a considerable increase in glycogen.

The causes of hyperplasia of the mucosa, which is chiefly seen at the time of puberty and the menopause, and seldom during the sexual period, were mentioned in part on p. 1628, as diseases of the uterus itself, diseases of the adnexa, changes in position, etc. (see Schickele and also Pankow). Others believe the chief cause is ovarian (Buttner, Hitschmann and Adler, Schroder, Aschner and others). Schroder believes one or more ripe follicles do not rupture and do not regress, and they stimulate the endometrium to prolonged proliferation. The hyperplastic mucosa shows bloody infarcts and necrotic particles (see p. 1629), and thus hemorrhages. If these ripe follicles are destroyed by x-rays, the proliferative stimulus ceases and atrophy overtakes the mucosa. The hemorrhages occur mostly after months of amenorrhea, (the failure of the follicle to progress to complete ripening does not allow the menstrual cycle to be completed), and are the most important clinical symptoms; these, however, are also present, among other things, with carcinoma. It is, therefore, easy to understand that curettage alone can have but little influence in these complicated processes, since the hyperplasia of the mucosa may be of ovarian origin.

Nodules of squamous epithelial cells, partly in hyperplastic glands in the mucosa of the body of the uterus and partly on the surface, merit attention since their interpretation is still uncertain, and it is not known whether or not they are beginning carcinomas. (Hunziker, R. Meyer, lit. and see p. 1625.)

Cervical Endometritis.—The inner surface of the cervix may show acute and chronic catarrh without involvement of the body of the uterus. The inflammation is usually spread from the vagina and is halted at the internal os.

Even gonorrhea is occasionally localized for a long time in the cervix without crossing the internal os, though this is not as frequent as was formerly supposed (Wertheim, see p. 1624). In other cases the cervical catarrh is part of a metritis and an endometritis which arose during childbirth or in the puerperium.

In chronic catarrh the mucous membrane is thickened and wavy; the tissue is infiltrated by cells. The secretion is usually glassy and mucoid, the dilated cellular glands grow into the depths of the infiltrated mucosa, even into the musculature, and the surface of the mucous membrane becomes sandy or papillary. Just as in the body of the uterus, there often appear circumscribed hypertrophies of the mucous membrane in the form of polyps; this may be called cervical polypoid endometritis, always remembering in this situation as well as in the other, that these independent structures may not be entirely free of inflammatory influences. Very frequent findings are small retention cysts as large as peas (Nabothian ovula), usually larger in the cervix than in the body (fig. 825). Stasis of secretion may be caused by these structures; on the other hand, increased secretion is concentrated and stretches the gland spaces which may also be dilated from obstruction of the ducts. Swelling of the ducts or constriction by scars following tears may also cause retention cysts. The cyst contents are glassy and colorless, cloudy white, or yellow with pus; the cysts themselves are transparent or cloudy from pus or blue to brown from blood. The author has occasionally seen very small laminated calcium bodies. In their further growth they force themselves to the surface when the surrounding tissue is soft; otherwise they are pushed downward and remain deep in the tissues. The latter circumstance is seen only in isolated cysts and seldom in larger complexes. The hyperplastic glands make the os look almost cavernous as it is thickly strewn with small mucus-containing cysts. This condition may give the impression of a tumor arising from the glands and infiltrating the tissues of the uterus. On the surface of the cervical canal, prominent cysts with some mucous membrane in the vicinity may be pressed out of their surroundings and so appear like cystic polyps; they may even develop true polyps and appear at the external os.

In relation to erosions of the cervix, to ectropion, and to hypertrophy of the cervix, see pp. 1634, 1635, 1636 and 1643.

The Etiology of Acute and Chronic Genuine and So-called Endometritis.—The acute forms and even the hemorrhagic types may occur during the acute infectious diseases such as measles, influenza, pneumonia, typhoid fever, etc.; others may be due to intra-uterine medication, others to septic infections in the puerperium, or to gonorrhea. The latter two may lead to chronic endometritis, but then the parasitic invaders can scarcely be demonstrated. Other chronic so-called spontaneous cases, as particularly frequent in chlorosis, have nothing to do with bacterial infection (Doederlein), even though bacteria may reach the uterus secondarily from the vagina. When the uterus secretes enough to neutralize the acid reaction of the vaginal secretions, bacteria, otherwise killed in the vaginal secretion, grow and infect the cervix. These conditions are favored by tears and by ectropion (see p. 1638). Cases of chronic so-called endometritis, or better, hyperplasia of the mucosa, with their chief symptom, metrorrhagia, often remain free of bacteria for a long time. They may be due to passive congestion of central or local origin from changes in position, tumors and so on (see p. 1628); an active hyperemia can be reflex from the ovaries. The so-called hyperplastic endometritis with myomas, formerly thought by many to be pure hyperplasia, also belongs in this category.

Other cases follow along in the puerperium or after an abortion. As the investigations of Winter and Puppe show, very early abortions (four to five weeks) may not be completely emptied; the ovum may be expelled and the decidua return again to uterine mucosa. This regression may be incomplete; the poorly involuted mucosa remains thickened with a tendency to hemorrhage, and this hyperplasia due to disturbed involution has been called decidual endometritis. It also happens after abortion that the decidua with its thickly packed polygonal cells persists only in certain focal places like islands in the mucosa (the glands disappear at these places), while the remainder of the mucosa is markedly infiltrated. For this also, a hyperplastic endometritis may be mistaken; in this condition there may be interstitial or glandular growths with prominent or broad based polyps or nodular hyperplasias of the mucosa, pictures which have been erroneously held characteristic of previous abortions (Opitz, see p. 1738). The condition has been given the name of decidual tuberous and polypoid endometritis. Even subchorion hematomas (see p. 1735) sometimes give the impression of polypoid decidual growths (Breus). If masses of the chorion remain behind and become hyalinized, they constitute a so-called placental polyp; p. 1739, figs. 872 and 873.

Circumscribed Hyperplasias (Polyps) of the Mucous Membrane.—Independent localized tumor-like growths of the mucosa of polypoid contour are very frequent and of varying appearance.

The border line between hyperplasia and tumor can not be sharply drawn, but polyps are not related in any way to diffuse hyperplasia.

In the body of the uterus they are usually soft (molluscum), and have broad bases; they are flat or hemispherical (fig. 824), often three-cornered through pressure by the uterine walls; they grow by preference in the corners. In the cervix, they are often tougher and have long pedicles.

(*Continued in Third Volume.*)

GENERAL INDEX TO VOLUMES I TO III

References in heavy-face type are to the pages containing illustrations. References in regular type are to the text and in italics to the volume.

Abdominal ascites, *i*, 176
Abortion, *iii*, 1737
Abscesses, bile, *i*, 290
  bone, *ii*, 1121, 1126
  brain, *iii*, 1828, **1902**, 1903, **1904**, **1906**
  cold, *ii*, 1126
  dental, *i*, 578
  Dubois, *i*, 502
  heart, *i*, **65**
  intestines, *i*, 764, *ii*, 830, 838
  joints, *ii*, 1235
  kidney, *ii*, 1361, 1364
  larynx, *i*, 313
  liver, *ii*, **881**, 913, **916**, **917**, 919
  lungs, *i*, 155, 411, 414
  parotid, *i*, 593
  perilaryngeal, *i*, 313
  peritoneum, *ii*, 876
  pharynx, *i*, 615
  portal, *ii*, **917**
  psoas, *ii*, 1128
  retropharyngeal, *i*, **616**
  spleen, *i*, **233**
  subphrenic, *i*, 233, 245, *ii*, 830
  teeth, *i*, 578
  testes, *ii*, 1484
  thyroid, *i*, 509
  tropical, *ii*, 915
  vertebrae, *ii*, 1131
Acardius, *i*, 86
Acarus follic, *iii*, 1807
  scabeii, *iii*, 2155, **2156**
Acephalus, *i*, 86
Achorion, *iii*, **2149**
Acne, *iii*, 2220
Acornus, *i*, 86
Acrania, *iii*, 1853
Acromegaly, *ii*, 1082, 1113, **1114**
  in hypophysis, *iii*, 1949
Actinomycosis of aorta, *i*, 17
  bones, *ii*, 1145, **1146**
  brain, *iii*, 1919
  esophagus, *i*, 638
  heart, *i*, 17
  intestines, *i*, 803
  jaw, *i*, **558**
  kidney, *ii*, 1374
  larynx, *i*, 320
  liver, *ii*, **944**
  lungs, *i*, 466
  mouth, *i*, 557
  parotid, *i*, 596
Actinomycosis of peritoneum, *i*, 15, *ii*, 872
  pharynx, *i*, 621
  pleura, *i*, **467**
  salivary glands, *i*, 596
  spine, *ii*, **1146**
  spleen, *i*, 243
  testes, *ii*, **1494**, *iii*, **1755**
  tongue, *i*, 559
  veins, *i*, 160
Adamantinoma, *i*, 585, **589**, **590**
Adams-Stokes symptom complex, *i*, 21
Addison's disease, *ii*, 1279, 1283
Adenoids, *i*, 301, 618
  of pharyng. tonsil, *i*, 606
Adenoma, bladder, *ii*, 1432
  breast, *iii*, **1772**
  goiter, *i*, 512
  hydradenoma, *iii*, **2200**
  intestines, *i*, 809
  kidney, *ii*, 1387, **1388**
  liver, *ii*, 954
  malignant, *iii*, **1682**
  pancreas, *ii*, 1022
  stomach, *i*, 690
  thyroid, *i*, 512
  uterus, *iii*, **1682**
Adeny-aleukemic, *i*, 265
Adhesions, intestinal, *i*, 744
  joints, *ii*, 1234, 1244, 1249
  laryngeal, *i*, 306
  pericardium, *i*, 17
  peritoneal, *ii*, 871
  pleura, *i*, 484
Adipose genital dystrophy, *iii*, 1952
Adiposis dolorosa, *iii*, 2179
Adrenalin, *ii*, 1278
Adrenals, *ii*, 1276
  accessory, *ii*, 1281
  Addison's disease, *ii*, 1279, 1283
  adrenalin, *ii*, 1278
  amyloid deg., *ii*, 1286
  anatomy, *ii*, 1276
  aplasia, *ii*, 1280
  chromaffin cells, *ii*, 1276, 1289
  cysts, *ii*, **1282**, 1289
  degenerations, *ii*, 1286
  development, *ii*, 1280
  ganglioneuroma, *ii*, 1288
  hemorrhages, *ii*, **1282**
  hypernephroma, *ii*, 1285, **1287**, 1289, 1290
  melania, *ii*, 1277
  melanoplakia, *ii*, 1284

Adrenals, misplaced adrenal rests, *ii*, 1291
  negri bodies, *iii*, 1901
  nerves, *ii*, 1277
  neuroblastoma, *ii*, 1288
  paraganglioma, *ii*, 1287, 1289
  parasites, *ii*, 1291
  pigmentation, *ii*, 1283
  removal, *ii*, 1281
  sarcoma, *ii*, 1289
  secretion, *ii*, 1278
  sex, *ii*, 1279
  softening, *ii*, 1281
  struma, *ii*, 1289
  syphilis, *ii*, **1286**
  testes, *ii*, 1481
  transplant, *ii*, 1281
  tuberculosis, *ii*, 1282, **1283, 1284**
  tumors, *ii*, 1287
  vascularization, *ii*, 1277
Agglutination (Widal), *i*, 785
Agnathia, *i*, 546
Agnesia, *iii*, 1859
Air embolism, *iii*, 1857
Albuminuria, *ii*, 1302
  juvenile, *ii*, 1325
Aleppo boil, *i*, 212
Aleucemia, *i*, 239, 624
Aleucemic adenia, *i*, **624**
Alkaptonuria, *ii*, 1230
Allantois, *ii*, 1422, *iii*, 1711
Alopecia, *iii*, 2221
Altmann granules, *i*, 194
Alzheimer's dis., *iii*, 1862
Ameba, intestinal, *i*, 772, *ii*, 847, **849,** 857
  of mouth, *i*, 560
Amnion, *iii*, 1710, 1711, 1714
  adhesions, *ii*, 1611, 1615
  fluid, *ii*, 1270, *iii*, 1719, 1720
  hydramnion, *iii*, 1720
Ampulla of Vater, *ii*, **998**
Amputation exostoses, *ii*, **1088**
  neuroma, *iii*, 2021
Amygdalitis, *i*, 606, 615
Amyloid deg. adrenals, *ii*, 1286
  arteries, *i*, 107
  bone, *ii*, 1221
  heart, *i*, 23, 55
  intestines, *i*, 758, 805
  kidney, *ii*, 1358, **1359**
  lymph nodes, *i*, 285
  pancreas, *ii*, 1038
  spleen, *i*, **243, 244**
  thyroid, *i*, 527
  vessels, *i*, 107
Amyloid infiltration of liver, *ii*, **903, 948**
Amyloid tumors, *i*, 323, 564
    in larynx, *i*, 326
    in leucemia, *i*, **263**
    mouth, *i*, 564
Amyotrophic lateral sclerosis, *iii*, 1995
Anasarca, *ii*, 1341
Anceps, *i*, 86
Anemia, *i*, 185
  ankylostoma, *i*, 190, *ii*, 854
  aplastic, *i*, 193
Anemia, Biermer's a., *i*, 189
  blood platelets, *i*, 187
  congenital hemolytic a., *i*, 192
  essential, *i*, 189
  heart, *i*, 55, 64
  intestines, *ii*, 851, 853
  kidney, *ii*, 1302
  liver diet, *i*, 191
  lungs, *i*, 370, 388
  parasites, *i*, 190
  pernicious, *i*, 189, **192**
  post mortem findings, *i*, 191
  a. pseudoleuc. infant., *i*, 193
  progressive, *i*, 189
  remission, *i*, 191
  sickle cell a., *i*, 193
  splenic a., 193, 223
  stomach, *i*, 661, 668, 713
Anencephalia, *iii*, 1852
Aneurysms, *i*, 116, **133,** 141, **149**
  aneurysmal varix, *i*, 148
  aorta, *i*, 4, **32,** 43, 93, **136, 146,** 647, *ii*, 1069
  arteries, *i*, **32,** 43, 123, 130, **133**
  arteriovenous, *i*, 32, **149**
  brain, *i*, 141, 147
  bruit, *i*, 134
  calcification, *i*, 135
  circoid a., *i*, 151
  congenital a., *i*, 150
  coronary, *i*, 4
  dissecting a., *i*, 134, 142, **144, 146, 149**
  duct of Botalli, *i*, **92**
  embolic a., *i*, 147
  erosion of bone, *i*, 135, 140, 148, *ii*, **1069,** 1087, 1214
  of heart, *i*, 32, 43, 56, 58, 69
  infections, *i*, 147
  intestinal, *i*, 757
  liver, *ii*, 899
  lungs, *i*, 145, 449
  miliary, *i*, 141
  nerve compression, *i*, 139
  perforating a., *i*, 145
  phlebarteriectasis, *i*, 150
  pseudo-a., *i*, 132
  rupture, *i*, 139
  sequellae, *i*, 139
  spleen, *i*, 229
  spontaneous a., *i*, 132, 134, 148
  syphilis, *i*, 135
  thrombi, 105, 116, 119
  traumatic a., *i*, 132, 142, 146
  true a., *i*, 132
  tuberculosis, *i*, 137, 450
  valvular a., *i*, **32,** 43, **58**
Angina Ludwig's, *i*, 614
  cynanche, *i*, 596
Angina pectoris, *i*, 55
Angina Plaut-Vincent, *i*, 550, 560, 613, 616
Angioma of bone, *ii*, 1201
  brain, *iii*, 1933
  cavernous, *i*, 151, *ii*, 952
  larynx, *i*, 323
  liver, *ii*, 852, 952
  racemose arterial, *i*, 151

Heavy face type denotes an illustration.

- Angigoma of vasa vasorum, *i*, 172
  - venous, *i*, 151
- Anguillula intest., *ii*, 854
- Anhydremia, *i*, 185
- Anidrosis, *iii*, 2221
- Anisocytosis, *i*, 192
- Ankylosis, *ii*, 1234, 1244
  - hipjoint, *ii*, **1263**
  - of knee, *ii*, **1263**
- Ankylostoma, *i*, 190, *ii*, 853, 854
- Annulus fibrosus, *i*, 41
- Anthracosis of lungs, *i*, 372, 418, 420, **474**
  - lymph nodes, *i*, 174, 250, 253, 254
  - lymphatics, *i*, 174
  - pericardium, *i*, 3, 5
- Anthrax, *i*, 213
  - in blood, *i*, 213
  - intestines, *i*, 803
  - lungs, *i*, 405
  - lymph nodes, *i*, 252
  - stomach, *i*, 670
- Antrum of Highmore, *i*, 295, 579, 591
- Anuria, *ii*, 1030, 1040
- Anus, *i*, 722, *iii*, 1701
  - artificial, *i*, 740
  - atresia, *i*, 723, **724**
  - and bladder, *ii*, 1424
  - embryology, *i*, 722
  - fissure, *ii*, 841
  - fistulae, *i*, 740, *ii*, 842
  - prolapsus, *i*, 741, 744
- Aorta, *i*, **24, 27, 32,** 45, 73, 93, **99,** 139, **146**
  - actinomycosis, *i*, 17
  - aneurysms, *i*, 4, **32,** 43, 93, **136, 146,** 320, 647, *ii*, 1069
  - arteriosclerosis, *i*, **108, 111**
  - atrophy, *i*, 150
  - calcification, *i*, **111**
  - congenital stenosis, *i*, 28, 47
  - dilatation, *i*, 116
  - hypertrophy, *i*, 151
  - lesions, *i*, 44
  - mesaortitis, *i*, 127, 137
  - sclerosis, *i*, 109
  - stenosis, *i*, 91
  - syphilis, *i*, 17, 56, 82, 123, **124, 125, 126, 128,** 131, **136**
  - tabes, *i*, 82
  - thrombi, *i*, **102**
  - trauma, *i*, 143, 146
  - tuberculosis, *i*, 17, 82, 131
  - valvular lesions, *i*, **31, 32,** 33, 42
  - vegetations, *i*, **29,** 35
- Apoplexy, *iii*, 1884, 1943
  - in pancreas, *ii*, 1024
  - in renal bed, *ii*, 1402
  - in uterus, *ii*, 1622
- Appendix vermiformis, *i*, 718, 747, 776, 816, *ii*, 832
  - appendicitis, *ii*, 832
  - carcinoma, *i*, **816,** *ii*, **817**
  - hydrops, *ii*, **839**
  - oxyuris vermicul, *ii*, **833**
  - perforation, *ii*, **837**
- Aprosopia, *i*, 547

- Apthae breast, *iii*, 1803
  - esophagus, *i*, **561,** 657
  - mouth, *i*, 549, 560, **561**
  - tongue, *i*, 560
  - vagina, *iii*, 1698
- Arachnoid, *iii*, 1804, 1960
- Argyll-Robertson sign, *iii*, 2004
- Argyria, *ii*, 1381
- Arsenic poisoning intest., *i*, 781
- Arteries, *i*, 89, 97, 99
  - adrenals, *ii*, 1277
  - amyloid deg., *i*, **107**
  - anatomy, *i*, 97
  - aneurysms, *i*, 32, 43, 45, 123, **133,** 150, 647
  - aorta, *i*, 73, **99,** 100, 107, 124, 139, 150, 647
  - arteriosclerosis, *i*, 105, 107, **108, 111, 112,** 115
  - arteritis, *i*, 117, 122, 131
  - atheroma, *i*, 23, 107, 110
  - atrophy, *i*, 150
  - bifurcation, *i*, 110
  - brain capillaries, *i*, **99,** 141, 142
  - bronchi, *i*, 339
  - calcification, *i*, **99,** 102
  - capillaries, *i*, 97, **99**
  - central retinal a., *i*, 119
  - coronary a., *i*, 55, 56, **57,** 107, 125
  - degenerations, *i*, 101, **106,** 107
  - diabetic gangrene, *i*, **104, 105,** 106
  - ductus arteriosus, *i*, 95, **97**
  - eclampsia, *i*, 151
  - embolism, *i*, 36, 41, 116, **119,** 152
  - endarteritis deformans, *i*, 117
  - endothelium, *i*, **99**
  - erosion, *i*, 123
  - fatty degenerat., *i*, **99,** 101
  - formation, *i*, 151
  - fracture, *i*, 105
  - gangrene, *i*, **104, 105, 106,** 120, 122
  - hyalin degen., *i*, 106
  - hypoplasia, *i*, 150
  - infections, *i*, 115, 190
  - intestinal, *i*, 749, 753, 756, *ii*, 845
  - mesarteritis, *i*, 121
  - nerves, *i*, 100
  - occlusion, *i*, 118, 381
  - organs of Zuckerkandl, *ii*, 1277
  - panarteritis, *i*, 120
  - periarteritis, *i*, 121
  - phlebarteriectasis, *i*, 150
  - plaques, *i*, 109
  - popliteal, *i*, 105
  - pulse, *i*, 3, 110
  - recanalization, *i*, 104, 121
  - renal, *ii*, 1303
  - retinal embolism, *i*, **119**
  - rose spots, *i*, 121, 781
  - sclerosis, *i*, 101, 103, 108, 109
  - senile gangr., *i*, 106
  - Sinus of Valsalva, *i*, 33
  - splenic, *i*, 226
  - stellate cells, *i*, **99**
  - stenosis, *i*, 151
  - syphilis, *i*, 123, **124, 125, 126, 128, 136, 137**
  - thrombosis, *i*, **102,** 105, 119

Heavy face type denotes an illustration.

Arteries, trauma, *i*, 152
  tuberculosis, *i*, 131
  tumors, *i*, 152
  vasa vasorum, *i*, **99,** 100, 112, 127, 172
  vascular formation, *i*, 151
  uterine, *i*, **106**
Arteriosclerosis aorta, *i*, **108, 111**
  brain, *i*, 107
  children, *i*, 114
  consequences, *i*, 116
  heart, *i*, 107
  kidneys, *i*, 107, 115, *ii*, **1312, 1314, 1315, 1331, 1351, 1353, 1355**
  lungs, *i*, 107
  metabolism, *i*, 115
Arteritis of aorta, *i*, 100, 107, 124
  gummatous, *i*, 129
  oblit., *i*, 120
  peri-, *i*, 121
  productive, *i*, 117
  tubercul., *i*, 131
Arthritis, *ii*, 1235
Arthritis deformans, *ii*, 1238, **1240,** 1242, **1245,** 1247, **1248**
Arthroma, *iii*, 2067
Arytenoid cartilage, *i*, 305, 313
Ascaris lumbricoides, *i*, 190, *ii*, **849,** 852, 1448
Ascites, causes, *i*, 176
  chylous, *i*, 176, 211, *ii*, 859, 872, 1566
Asphyxia, *i*, 382
Aspiration-pneumonia, *i*, 406, 414
Asteatosis, *iii*, 2216
Asthma bronchial, *i*, 344
  eosinophiles, *i*, 197, 278, 344
  thymic, *i*, 499
Ataxia heredit., *iii*, 2005
Atelectasis of lungs, *i*, 359, 361
Atelectatic bronchiectasia, *i*, 355
Atheroma of arteries, *i*, 107, 110
  dermoid atheroma, *iii*, **2218**
  of heart, *i*, 20, 23
  skin, *iii*, 2217
Athyreosis, *i*, 508
  congenit., *ii*, **1182**
Atlas, *ii*, 1131
Atresia of anus, *i*, 722, 747
  esophagus, *i*, 632
  intestinal, *i*, 723, **724,** 747
Atrioventricular system, *i*, 20
Atrophy of aorta, *i*, 150
  arteries, *i*, 151
  bladder, *ii*, 1428
  bone, *ii*, **1052,** 1063, **1065,** 1067, **1068, 1069**
  brown a., *i*, 49
  gall bladder, *ii*, 1000
  heart, *i*, 49, 73
  intestines, *i*, 804
  kidney, *ii*, 1310, **1311,** 1314, **1315,** 1331
  kidney granular, *ii*, 1310
  liver, *ii*, 901
  marantic, *ii*, 1067
  neurotic, *ii*, 1070
  pancreas, *ii*, 1037
  pressure, *ii*, 1068
  seminal vesicles, *ii*, 1517

Atrophy of stomach, *i*, 667
  testes, *ii*, 1510, 1517
  thymus, *i*, 498
  yellow, *ii*, 907
Auerbach's plexus, *i*, 719
Auricles, *i*, 21, 78, 87
Autointoxication, *i*, 190

BACTEREMIA, *i*, 213
Bacteria and their locat., anus, *ii*, 845
  anthrax, *i*, 213, 252, 405, 670, 803
  bladder, *ii*, 1426, 1452
  in blood, *i*, 213
  bone, *ii*, 1096, 1121, 1235
  botulinus, *i*, 762
  bovine tuberculosis, *i*, **490,** *iii*, 1832
  breast, *iii*, 1761
  bronchi, *i*, 341, 347
  cervix, *ii*, 1631
  chancre soft, *ii*, 1534
  cholecyst, *ii*, 981, 989
  cholera, *i*, 777
  colon, *i*, 718
  diphtheria, *i*, 61, 65, 294, 311, 312, 319, 343, 560, 607, 608, 611, 636, 768, 774, *ii*, 1316, 1329, 1338, 1364, *iii*, 1702
  diplococcus lanceolat, *i*, **394**
  Ducrey's, *ii*, 1534
  edema malign, *iii*, **2042, 2043, 2044, 2045**
  endocardium, *i*, 15, 33, **34,** 35
  esophagus, *i*, 636
  Fallop. tubes, *ii*, 1594
  fission fungi, *i*, 213
  Fraenkel-Weichselbaum dipl., *i*, 394
  Friedlander's, *i*, 295
  gall bladder, *ii*, 981, 989
  gas bac., *iii*, **2042, 2043, 2044, 2045**
  glanders, *i*, 130, 175, 213, 243, 252, 298, 320, 559, 621, *ii*, 945, 1494
  gonococcus, *ii*, 1449
  gonorrhea in children, *iii*, 1693
  heart, *i*, 15, 26, 28, 31, 33, 35, 38, 61, 65
  influenza, *i*, 296, 309, 341
  intestines, *i*, 751, 760, 768, 773, 774, 783, 803, *ii*, 845, 858
  joints, *ii*, 1237
  kidney, *ii*, 1316, **1329,** 1338, 1364
  larynx, *i*, 309, 311, 319
  leprosy, *i*, 62, 243, 262, 299, 319, 557, *ii*, 846, *iii*, 2146
  lungs, *i*, 386, 389, 406, 428, 805
  lymph nodes, *i*, 212, 252, 255, 262
  lymphatics, *i*, 173
  meningococcus, *iii*, 1830
  mouth, *i*, 516, 548, 550
  nose, *i*, 292, 294, 295, 299
  ozena, *i*, 295
  palate, *i*, 311
  paratyphoid, *i*, 761
  parotid, *i*, 593
  penis, *ii*, 1493, 1534
  pericarditis, *i*, 15
  peritonitis, *ii*, 860, 867
  pertussis, *i*, 309
  pestis, *i*, 252, 253, 406

Bacteria and their locat., pharynx, *i*, 607, 608, **611**
  placenta, *iii*, 1732
  plague, *i*, 252, 253, 406
  pneumonia, *i*, 388, **394**
  prostate, *ii*, 1449
  puerperium, *iii*, 1749, 1755
  rectum, *ii*, 845
  rhinoscleroma, *i*, 300
  scleroma, *i*, 301, 621
  smegma, *ii*, 1534
  staphylococcus, *iii*, 2104
  streptococcus viridans, *i*, 34, 36
  teeth, *i*, 579
  testes, *ii*, 1494
  tongue, *i*, 559
  tonsils, *i*, 309, 311, 319
  tuberculoids, *iii*, 2118
  tuberculosis, *i*, 17, 47, 72, 82, 131, 159, 213, **241**, 255, 297, 315, 333, 340, 343, 348, 349, 351, 416, 422, 443, 444, 489, 529, 544, **555**, 580, 619, **620**, 637, 644, 670, 796, **799**, **800**, *ii*, 861, 870, **934**, **935**, 1001, 1033, **1052**, 1122, **1124**, **1125**, **1126**, **1127**, **1129**, **1130**, **1132**, 1245, 1255, **1256**, **1260**, 1282, **1283**, **1284**, 1308, 1322, 1365, 1366, **1369**, **1371**, 1415, 1430, 1431, 1454, **1487**, 1490, **1598**, *iii*, **1639**, 1640, **1675**, 1832, 1833, **1835**, **1836**, **1905**, **1914**, **1915**, 2127
  tuberculosis attenuated, *i*, 256
  tularemia, *i*, 262
  urethra, *ii*, 1449
  uterus, *ii*, 1631, *iii*, 1718, 1732, 1748
  vagina, *iii*, 1691
  vulva, *iii*, 1702, 1703
Balanitis, *ii*, 1533
Balanoliths, *ii*, 1540
Balantidium, *ii*, 857
Banti's disease, *i*, 224
Barlow's disease, *ii*, 1166
Bartholin's duct, *i*, 575
  glands, *iii*, 1702, 1770
Basedow's disease, *i*, 516, **519**
  and thymus, *i*, 501
Basophiles, *i*, 195
Basophilic degeneration, *i*, 188, 551
Bedbug, *iii*, 2155
Beri-Beri, *iii*, 2016
Biermer's anemia, *i*, 189
Bile, *ii*, 885, 893, 999
Bile abscess, *ii*, 920
Bile capillaries, *ii*, 1011, 1016
Bile ducts, *ii*, 979
  inflammation, *ii*, 981
  occlusion, *ii*, 997, 999
  tumors, *ii*, 1007
Bile peritonitis, *ii*, 864
Bile pigments, *i*, 192, *ii*, 987, 1011, 1013
Bile stasis, *ii*, 990, 1011, 1013
Bile thrombus, *ii*, **1014**
Bilharzia hematobia, *i*, 190, 211, *ii*, 856, 1447
Bilirubin production by kidney, *ii*, 1376
  by spleen, *i*, 219
Birth trauma, *iii*, 1810, 1811
Birthmarks, *i*, 171
Black water fever, *i*, 186
Bladder, urinary, *ii*, 1296, 1421, 1424, 1458
  abscesses, *ii*, 1429
  adenoma, *ii*, 1432
  allantois, *ii*, **1422**
  atrophy, *ii*, 1429
  bacteria, *ii*, 1426
  calculi, *ii*, **1411**, **1412**, 1424, **1440**
  carcinoma, *ii*, 1423, 1432, **1435**, 1436, 1439, *iii*, 1697
  circulat., *ii*, 1425
  cloaka, *ii*, 1424
  cystitis, *ii*, 1426, 1528
  cystocele, *ii*, 1427
  cysts of urachus, *ii*, 1422
  dilatation, *ii*, 1443
  diphtheria, *ii*, 1429
  diverticuli, *ii*, **1444**, **1445**
  ectopy, *ii*, 1424
  edema, *ii*, 1425
  extrophy, *ii*, **1423**
  fistulas, *ii*, 1432
  foreign bodies, *ii*, 1447
  gas, *ii*, 1430
  glands, *ii*, 1421
  hematuria, *ii*, 1528
  hemorrhage, *ii*, 1425
  hypertrophy, *ii*, **1443**, **1523**, 1528
  inflammation, *ii*, 1426
  malakoplakia, *ii*, 1428
  malformation, *ii*, 1422
  necrosis, *ii*, 1425
  papilloma, *ii*, 1432, **1433**, **1434**
  paracystitis, *ii*, 1429
  parasites, *ii*, 1447
  pelvis, cleft, *ii*, 1424
  perforation, *ii*, 1429
  peritonitis, *ii*, 1430
  polyps, *ii*, 1431
  polyuria, *ii*, 1529
  position changes, *ii*, 1446
  prostate, *ii*, 1421, 1431, 1448, 1453
  retroversion of uterus, *ii*, 1611
  rhabdomyoma, *ii*, **1437**
  rupture, *ii*, 1446
  sarcoma, *ii*, **1438**
  syphilis, *ii*, 1432
  testes, *ii*, 1431
  trauma, *ii*, 1446
  tuberculosis, *ii*, 1430
  tumors, *ii*, 1424, 1432, **1433**, **1434**, **1435**, **1437**
  ulcers, *ii*, 1428, 1432
  urachus, *ii*, 1422
  ureters, *ii*, 1459
  urethra, *ii*, 1449
  vesicles semin., *ii*, 1431, 1515
Blandin-Nuhn's gland, *i*, 575
Blastomas, *i*, 266
Blastomycosis, *ii*, 1147, *iii*, 2154
Blennorrhea ophthalm., *ii*, 1453
Blood, *i*, **200**
  absorption, *i*, 185, *ii*, 861
  air in circulat., *i*, 207
  aleucemia, *i*, 206

Heavy face type denotes an illustration.

Blood, anemia, *i*, 185, 192
  anemia aplastic, *i*, 193
    pernicious, *i*, 189
    sickle cell, *i*, 193
    splenic, *i*, 193
  anhydremia, *i*, 185
  anisocytosis, *i*, 192
  anthrax, *i*, 213
  autointoxication, *i*, 190
  bacteremia, *i*, 213
  basophiles, *i*, 195
  basophilic degeneration, *i*, 188, 551
  bilharzia, *i*, 190
  blackwater fever, *i*, 186
  blood diseases, *i*, 189
  blood making organs, *i*, 216, 286
  blood-platelets, *i*, 186
  carbon monoxide poisoning, *i*, 215
  carcinoma, *i*, 190
  Chaga's disease, *i*, 212
  changes in blood, *i*, 185
  chlorosis, *i*, 187, 189
  coagulation, *i*, 186
  eosinophiles, *i*, 197
  epistaxis, *i*, 293
  erythemia, *i*, 189
  erythroblasts, *i*, 188, 286
  erythrocytes, *i*, 186, 187
  erythrocytophagia, *i*, 219
  fat emboli, *i*, 207
  fever recurrent, *i*, 215, 782
  filaria, *i*, 210, **211**
  fission fungi, *i*, 213
  foreign bodies, *i*, 206
  glanders, *i*, 213
  hemoconia, *i*, 188
  hemoglobin, *i*, 189
  hemoglobinemia, *i*, 186
  hemoglobinuria, *i*, 186
  hemolysin, *i*, 190
  hemophilia, *i*, 186
  hemorrhages, *i*, 204
  hemorrhagic diatheses, *i*, 201
  Hodgkin's disease, *i*, 193
  Howell-Jolly bodies, *i*, 188
  hydremia, *i*, 185
  hyperinosis, *i*, 186
  hypoinosis, *i*, 186
  icterus-, *i*, 186
    (familial), *i*, 192
    (infectious), *i*, 214
  impurities, *i*, 206
  kala azar, *i*, 212
  lead poisoning, *i*, 188, 551
  leucemias, *i*, 187, 191, 198, 205
  leucemic infiltration, *i*, 204
  leucocytes, *i*, 194
  leucocytosis, *i*, 197
  leucopenia, *i*, 198
  louse, *i*, 213
  lymph, *i*, 215
  lymphocytes, *i*, 194
  lymphoma, *i*, 203
  lymphopenia, *i*, 187
  macrocytes, *i*, 188
Blood, malaria, *i*, 190, 208, **209**
  mast cells, *i*, 195
  megacaryocytes, *i*, 187
  melanemia, *i*, 204
  melanin, *i*, 210
  methemoglobin, *i*, 187
  microcytosis, *i*, 188
  myeloblasts, *i*, 194
  myelocytes, *i*, 190, 198
  myelosis, *i*, 206
  normoblasts, *i*, 188
  oligocythemia, *i*, 185, 187
  organs hemopoietic, *i*, 216, 286
  osteomyelitis, *i*, 190
  osteosclerosis, *i*, 204
  oxidase reaction, 196
  parasites, *i*, 190, 208
  pest bacilli, *i*, 213
  Peyer's patches, *i*, 203
  pigments, *i*, 206, 371, *ii*, 1106, 1309, 1377
  platelets, *i*, 186
  pneumonatemia, *i*, 207
  poikilocytosis, *i*, 192, **200**
  poisons, *i*, 186, 190, 215
  polychromatophilia, *i*, 192
  polycythemia, *i*, 187
  postmortem changes, *i*, 189
  pseudoleucemia, *i*, 205
  quality changes, *i*, 185
  quantity, *i*, 185
  shape of cells, *i*, 188
  sickle cells, *i*, 194
  sleeping sickness, *i*, 211
  spirillae, *i*, 214, 782
  spirochetae, *i*, 214
  syphilis, *i*, 190, 215
  tetanus, *i*, 213
  tick infection, *i*, 212
  thrombocytes, *i*, 186
  thrombokinase, *i*, 189
  thymus, *i*, 189
  toxins, *i*, 190, 208
  transfusion, *i*, 185
  trichinae, *i*, 211, 212, *iii*, **2056**
  trypanosoma, *i*, 211, **212**
  tuberculosis, *i*, 213
  tularemia, *i*, 262
  typhus, *i*, 213
  uremia, *ii*, 1300, 1310, 1342
  Vagues-Osler disease, *i*, 189
  vegetable parasites, *i*, 213
  volume changes, *i*, 186
  Weil's disease, *i*, 214, 219
  yellow fever, *i*, 214
Bloodmole, *i*, 171, *iii*, 1736
Bochdalek's duct, *i*, 507
Boils, *i*, 212, *iii*, 2107, 2158
Bone, *ii*, 1051
  abscess, *ii*, 1121, 1126, 1127, 1131
  absorption, *ii*, **1052**
  acromegaly, *ii*, 1082, 1113, **1114,** 1187
  actinomycosis, *ii*, 1145, **1146**
  amputation stump, *ii*, **1088**
  amyloidosis, *ii*, 1221
  anatomy, *ii*, 1151

Heavy face type denotes an illustration.

Bone, aneurysm, *ii*, 1069, 1214
  angioma, *ii*, 1201
  athyreosis, *ii*, 1182
  atlas, *ii*, 1131
  atrophy, *ii*, 1052, 1063, 1065, **1069**
    marantic, *ii*, 1067
    pressure, *ii*, 1068
    senile, *ii*, **1065, 1068**
  bacteria, *ii*, 1096
  blastomycosis, *ii*, 1147
  bone changes, *ii*, 1060
  bone formation, *ii*, 1056, 1057
  bone marrow, *i*, 286
  brachycephalia, *ii*, 1189
  calcium, *ii*, 1052, 1064, 1068, 1135, 1157
  callus, *ii*, 1055, 1085, 1086, 1087, 1177
  callus cysts, *ii*, 1088
  canalization, *ii*, 1053
  carcinoma, *ii*, 1120, 1194, **1222, 1224**
  caries, *ii*, 1103, 1123, **1130,** 1131, **1138,** 1139
  cartilage, *ii*, 1062, 1229
  caseation, *ii*, 1105
  castration, *ii*, 1186
  cephalic hematoma, *ii*, **1092,** 1093
  chloroma, *ii*, 1221
  chondrodystrophy, *ii*, 1170, **1172, 1173**
  chondroma, *ii*, 1201
  clubbed fingers, *ii*, 1115
  congenital syphilis, *ii*, 1102
  consolidation, *ii*, 1089
  coxavara, *ii*, 1072, 1272
  coxitis, *ii*, 1132
  craniotabes, *ii*, 1156, 1165
  cretinism, *i*, 523, *ii*, 1181, 1182, 1183, **1185**
  cysts, *ii*, **1226**
  deformities, *ii*, 1072, 1079
  demarkation, *ii*, 1116
  diaphysis, *ii*, **1058, 1117,** 1152, 1177
  dislocations, *ii*, 1086, 1090
  disturbance of growth, *ii*, 1169
  dolichocephalia, *ii*, 1189
  drumstick fingers, *ii*, 1082
  dwarfism, *ii*, 1179
  dysostoses, *ii*, 1198
  eburnation-exostosis, *ii*, 1195
  ecchondrosis, *ii*, **1196**
  echinococcus, *ii*, 1227
  enchondromas, *ii*, 1194, 1198, **1200, 1202, 1204, 1205**
  endosteum, *ii*, 1152, 1157, **1158, 1159**
  epiphysis, *ii*, **1059,** 1137, 1155, 1171
  epistropheus, *ii*, 1131
  epulis, *ii*, 1215
  erosion, *i*, 135, 140, 148, *ii*, 1069, 1087, 1214
  exostoses, *ii*, 1083, **1088,** 1195, **1197,** 1198, **1199,** 1275
  fetal bone, *ii*, 1054
  fibroblasts, *ii*, 1052
  fibromas, *ii*, 1200
  fingers, (clubbed), *ii*, **1115**
    drumstick, *ii*, 1082
  fissures, *ii*, 1084
  fontanelles, *ii*, 1164
  formation of bone, *ii*, 1055, **1060**
  fractures, *ii*, 1081, **1085,** 1089, **1090, 1225**

Bone, fractures spontaneous, *ii*, 1067, 1227
  genu valgum, *ii*, 1072, 1244
  gigantism, *ii*, 1082, 1150, 1186
  gomphosis, *ii*, 1090
  granulamas, *ii*, 1122
  greenstick fracture, *ii*, 1083
  halisteresis, *ii*, 1055, 1080
  Haversian canals, *ii*, 1056
  healing, *ii*, 1081, 1083
  hemangioma, *ii*, 1201
  hemangiosarcoma, *ii*, 1212
  hemiatrophy of face, *ii*, 1070
  hydrocephalus, *ii*, 1165, **1166**
  hypernephroma, metastatic, *ii*, 1225
  hyperostosis, *ii*, 1083, 1107, 1112
    syphilitic, *ii*, 1142
  inflammation, *ii*, 1084, 1091
  kyphosis, *ii*, 1066, 1079, **1129,** 1163
  lacunae, *ii*, 1065
  lattice figures, *ii*, 1055
  leontiasis, *ii*, **1112**
  leprosy, *ii*, 1147
  leucocytoma, *ii*, 1220
  lipoma, *ii*, 1201
  lipomacia, *ii*, 1063
  lordosis, *ii*, 1079, 1163
  luxations, *ii*, 1268
  lymphangioma, *ii*, 1201
  lymphocystoma, *ii*, 1220
  macrocephalia, *ii*, 1189
  macrosomia, *ii*, 1186
  malacia, *ii*, 1072
  malformations, *ii*, 1072, 1179, 1189
  marrow, *i*, 286, *ii*, 1111
  marrow-tumors, *ii*, 1169
  metaplasia, *ii*, 1061, 1084
  metastases, *ii*, 1101
  microcephalia, *ii*, 1189
  micromelia, *ii*, 1169, **1178**
  micromelus, *ii*, **1170**
  Moller-Barlow disease, *ii*, 1166, **1168**
  myelocystoma, *ii*, **1219**
  myelogenous sarcoma, *ii*, **1191, 1192,** 1210, **1214**
  myeloma, *ii*, **1218**
  myelomalacia, *ii*, 1130
  myxoma, *ii*, 1200
  Naegeli's pelvis, *ii*, 1078, 1188
  nannosomia, *ii*, 1179
  nearthrosis, *ii*, 1086, 1089
  necrosis, *ii*, 1062, 1116, **1117, 1118, 1119, 1121,** 1139
  neurotic atrophy, *ii*, 1070
  organisms, pathogenic, *ii*, 1096, 1121, 1235
  ossification, *ii*, 1150, 1155, 1161, 1190
  osteoblasts, *i*, 286, *ii*, 1056
  osteochondritis, *ii*, 1137
  osteoclasts, *ii*, 1056
  osteocytes, *ii*, 1056
  osteofibroma, *ii*, **1194**
  osteogenesis imperfecta, *ii*, 1064, **1175, 1176, 1178**
  osteoid tissue, *ii*, 1152, 1208
  osteoidchondroma, *ii*, 1206
  osteolysis, *ii*, 1071

- Bone, osteoma, *ii*, 1195, 1199, *iii*, 2053
  - osteomalacia, *ii*, 1054, 1062, 1064, 1071, **1073,** 1076, 1154
  - osteomalacia puerperal, *ii*, **1076,** 1077, 1164
  - osteomyelitis, *ii*, 1095, 1097, 1101, 1103
  - osteomyelitis metastatic, *ii*, **1100,** 1101
  - osteophytes, *ii*, **1092,** 1121, 1152
  - osteoplast, *i*, 286, *ii*, 1082
  - osteoporosis, *ii*, 1067, 1108
  - osteopsathyrosis, *ii*, 1063, 1177
  - osteosarcoma, *ii*, 1208
  - osteosclerosis, *ii*, **1106**
  - ostitis, *ii*, 1095, 1103, **1110,** 1114, **1226**
  - ostitis deformans, *ii*, 1107, 1145
  - ostitis ossific, *ii*, 1106, 1128
  - Paget's disease, *ii*, 1107, **1108**
  - parasites, *ii*, 1227
  - pelvis, *ii*, **1078,** 1162, 1164, 1175, 1188, 1267, 1278
  - periosteum, *ii*, 1057, 1148
  - periostitis, *ii*, 1092, 1097, **1100,** 1101, 1114, 1121
  - periostitis syphil., *ii*, 1137
  - phosphorus necrosis, *ii*, 1083, 1106, 1120, 1121
  - Pott s disease, *ii*, **1129, 1132**
  - pseudo arthrosis, *ii*, 1089, 1191
  - psoas abscess, *ii*, 1128
  - rachischisis, *ii*, 1 65
  - rachitis, *ii*, 1151, **1153,** 1155, **1156, 1162,** 1163
  - regeneration, *ii*, 1081
  - regression, *ii*, 1062
  - resorption, *ii*, 1055, 1154
  - ribs, *ii*, 1131, 1151
  - rickets, *ii*, 1151, 1153, 1155, 1156, 1162, 1163
  - sarcoma, *i*, 43, *ii*, **1191, 1192, 1193, 1194, 1207, 1209, 1210, 1211, 1212, 1213, 1214, 1226**
  - sclerosis syphil, *ii*, 1143
  - scoliosis, *ii*, 1066, 1079
  - sequestra, *ii*, 1117, **1118,** 1121, 1126
  - Sharkey s fibres, *ii*, 1056
  - skeletal defects, *ii*, 1161, 1169
  - skull, *ii*, 1065, 1093, **1112, 1114,** 1131, **1138, 1140, 1141, 1143,** 1144, **1163,** 1164, **1193, 1199, 1218**
  - spina ventosa, *ii*, 1128
  - sporotrichosis, *ii*, 1147
  - synostoses, *ii*, 1172, 1188
    - premature, *ii*, 1188
  - syphilis, *ii*, 1102, 1133, **1134, 1136, 1138, 1139, 1140, 1141, 1142, 1143**
    - congenit., *ii*, 1133, **1136**
  - trauma, *ii*, 1102, 1145, 1195, 1216
  - tuberculosis, *ii*, 1122, **1124, 1126, 1127, 1130,** 1131
    - pus, *ii*, 1123
  - tumors, *i*, 291, *ii*, 1192, 1216
  - typhoid, *ii*, 1096
  - vertebrae, *ii*, 1060, 1071, **1127, 1129, 1132,** 1145, 1146, 1163
  - Volkman s canals, *ii*, 1053
- Bone marrow, *i*, 286
- Bone marrow, in anemia (pernicious), *i*, 193
  - cells, *i*, 188, 190, 194, 286
  - changes, *i*, 288, *ii*, 1111
  - color, *i*, 288
  - erythroblasts, *i*, 191, 287
  - in exostoses, *ii*, 1195
  - fat marrow, *i*, 288
  - fibrous marrow, *ii*, 1111
  - function, *i*, 194
  - giant cells, *i*, 286
  - in infectious diseases, *i*, 290
  - leukemias, *i*, 204, 288
  - marrow-callus, *ii*, 1084
  - Muller Barlow s disease, *ii*, 1167
  - myelomas, *i*, 291, *ii*, 1219
  - osteomalacia, *ii*, 1077
  - red marrow, *i*, 288
  - stimulation, *i*, 188
  - tumors, *i*, 168, 291, *ii*, 1193, 1219
  - veins, *i*, 159
  - x-ray injury, *i*, 193
  - yellow marrow, *i*, 287
- Botalli's ductus arteriosus, *i*, 95, 97
- Bothriocephalus latus, *i*, 190, *ii*, **849,** 850
- Botulism, *i*, 762
- Bovine tuberculosis, *i*, **490,** *iii*, 1832
- Brachycephaly, *ii*, 1189
- Brain, *iii*, 1852
  - abscess, *iii*, 1828, **1902,** 1903, **1904, 1906**
    - metastatic, *iii*, 1903, **1904, 1906**
  - absense of corpus callosum, *iii*, 1859
  - acrania, *iii*, **1848**
  - actinomycosis, *iii*, 1919
  - agnesia, *iii*, 1859
  - Alzheimer's disease, *iii*, 1862
  - ameboid glia, *iii*, 1877
  - anemia, *iii*, 1879, 1894
  - anencephalia, *iii*, 1852
  - aneurysms, *i*, 141, 147, *iii*, 1890
  - angiomas, *iii*, 1933
  - apoplexy, *iii*, 1884, 1943
  - arteries, *i*, 100, 104, 109, 141, 142, *iii*, 1891 **1893**
  - arteriosclerosis, *i*, 109, 142, *iii*, 1894
  - atrophy, *iii*, 1862, 1869
  - autopsy findings, *iii*, 1863
  - bacteria, *iii*, 1898, 1900
  - birth trauma, *iii*, 1849, 1860
  - calcificat., *iii*, 1878
  - capillaries, *i*, **99**
  - carbon monoxide poisoning, *iii*, 1898
  - carcinoma, *iii*, 1934
  - cephalhematoma, *iii*, 1810
  - cerebrospinal fluid, *iii*, 1805, 1846
  - cerebrospinal meningitis, *iii*, 1830
  - cerebrum, *iii*, 1852
  - cholesteatoma, *iii*, **1840**
  - chorionepithelioma metast., *iii*, **1935**
  - chromatophores, *iii*, 1843
  - circulatory disturbances, *iii*, 1879
  - compression, *iii*, 1940
  - concussion, *iii*, 1941
  - corpus callosum, *iii*, 1883, 1859, 1913
  - cysticercus, *iii*, **1845,** 1938
  - cysts, *iii*, 1935

Heavy face type denotes an illustration.

- Brain, degenerations, *iii*, 1870, 1872, 1876
  - dementia (paralytica), *iii*, 1864
    - senile, *iii*, 1862
  - dura, *iii*, 1894
  - echinococcus, *iii*, 1938
  - edema, *iii*, 1862
  - embolism, *iii*, 1891, **1893**
  - encephalitis, *iii*, 1894, 1899, 1901, 1902, 1907
    - lethargic, *iii*, 1899, 1901
    - neonatorum, *iii*, 1901
  - endarteritis obliterans, *i*, **130**
  - fat granule cells, *iii*, **1871**
  - fibro endothelioma, *iii*, **1817**
  - focal degenerat., *iii*, 1869
  - focal symptoms, *iii*, 1937
  - ganglion cell changes, *iii*, 1870
  - ganglion neuromas, *iii*, 1931
  - gas poisoning, *iii*, 1873
  - gliomas, *iii*, 1921 to 1930, 1932
  - glioses, *iii*, 1908
  - gumma, *iii*, **1842**
  - hematoma, *iii*, **1813**
  - hemicephalia, *iii*, **1843,** 1853
  - hemiplegia, *iii*, 1869
    - spastica, *iii*, 1869
      - infant., *iii*, 1869
  - hemorrhage, *i*, 142, *iii*, **1807,** 1881, 1882, **1883, 1885, 1887, 1922**
  - hernia, *iii*, **1855**
  - heterotopia, *iii*, 1861
  - hydrencephalocele, *iii*, **1854**
  - hydrocephalus, *iii*, 1823, **1826,** 1828, 1832, **1847,** 1848, 1849, **1854**
  - hydrophobia, *iii*, 1900
  - hygroma, *iii*, **1814**
  - hyperemia, *iii*, 1879
  - hypoplasia, *iii*, 1852
  - lethargic encephalitis, *iii*, 1899, 1901
  - lumbar puncture, *iii*, 1830
  - malaria, *i*, 210, *iii*, 1919
  - malformations, *iii*, 1852, **1853** to **1857**
  - medulla oblongata, *iii*, 1843
  - melanoma, *iii*, 1843
  - meninges, *iii*, 1804, 1810
  - meningitis, *iii*, 1828
  - microcephalia, *iii*, 1853, **1856, 1857**
  - microencephalitis, *iii*, **1856, 1857**
  - microgyria, *iii*, 1858
  - Negri bodies, *iii*, 1900
  - nerve fibre changes, *iii*, 1874
  - neuronophagia, *iii*, 1872
  - Nissl bodies, *iii*, 1872
  - panophthalmia, *iii*, 1809
  - paralysis, (acute bulbar), *iii*, 1993
    - juvenile, *iii*, 1867
  - parasites, *iii*, 1938
  - Parkinson's disease, *iii*, 1913
  - passive congestion, *iii*, 1880
  - poisoning, *iii*, 1873, 1898, 1912
  - polioencephalomyelitis, *iii*, 1899
  - porencephalia, *iii*, 1860
  - post mortem findings, *iii*, 1863
  - pressure, *iii*, 1937, 1940
  - progressive, *iii*, **1866,** 1995
- Brain, progressive lenticul. degenerat., *iii*, 1863
  - psammoma, *iii*, **1816**
  - rabies, *iii*, 1900
  - sarcoma, *iii*, 1932, 1934
  - sclerosis, *iii*, 1892, 1907, **1910,** 1911, 1932
  - senile dementia, skull, *iii*, 1852
  - softening, *iii*, 1862, **1894**
  - spinal nerves, *iii*, **1960**
  - spotted fever, *iii*, 1920
  - swelling, *iii*, 1861
  - syphilis, *iii*, 1864, 1901, 1915
  - thrombosis, *iii*, 1892
  - tigroid cells, *iii*, 1872
  - traumas, *iii*, 1822, 1849, 1860, 1903, 1941, 1943, 1944
  - tuberculosis, *iii*, 1832, 1833, **1914, 1915**
  - tumors, *iii*, 1908, 1920, 1932, 1934, 1963
    - of lymphatics, *i*, 181
  - ventricles, *iii*, 1846, 1928
  - Wilson's disease, *iii*, 1863
  - wounds, *iii*, 1944
- Branchiogenic carcinoma, *i*, 330, **331**
  - clefts, *i*, **328,** 329
  - cysts, *i*, 327, 576
  - fistulas, *i*, 329, **506**
  - tumors, *i*, 330
- Breast, *iii*, 1756
  - aberrant, *iii*, 1760
  - abnormal involution, *iii*, 1766, **1767**
  - abscess, *iii*, 1762, 1769
  - actinomycosis, *iii*, 1763, 1770
  - adenofibroma, *iii*, **1776, 1777, 1778**
  - adenoma, *iii*, 1770, **1772, 1773**
  - amastia, *iii*, 1759
  - amputation, *i*, **118**
  - anatomy, *iii*, 1757
  - axillary lymph nodes, *iii*, 1797, 1799
  - bacteria, *iii*, 1762
  - bleeding nipple, *iii*, 1761, 1782
  - carcinoma, *i*, **118,** *iii*, 1763, 1766, 1768, **1780, 1785,** 1786, **1788, 1789, 1791, 1792, 1793, 1794, 1795, 1796, 1797, 1800**
  - circulatory disturbances, *iii*, 1761
  - cirrhosis, *iii*, 1763
  - colostrum, *iii*, 1758
  - cystadenoma, *iii*, 1765, 1768, **1779**
  - cystic breast, *iii*, 1764
  - cysticercus, *iii*, **1803**
  - cystosarcoma, *iii*, **1781**
  - cysts, *iii*, 1766, 1802
  - echinococcus, *iii*, 1803
  - embryology, *iii*, 1756
  - fibroadenoma, *iii*, 1774, **1775, 1776, 1777, 1778**
  - fistula, *iii*, 1769
  - galactocele, *iii*, 1765, 1802
  - galactorrhea, *iii*, 1771
  - glands, *iii*, 1759
  - gynecomastia, *iii*, 1759, **1760, 1783**
  - hemorrhages, *iii*, 1761
  - hypertrophy, *iii*, 1770, 1771
  - infection, *iii*, 1761
  - inflammation, *iii*, 1761, **1764,** 1767

Breast, involution, *iii*, 1763, 1766
  involution, abnormal, *iii*, **1767**
  involution-cysts, *iii*, 1766
  lactat. in male, *iii*, 1758
  lactation, *iii*, **1757,** 1766
  lipoma in male breast, *iii*, **1783**
  macromastia, *iii*, 1759, 1770
  male breast, *iii*, 1758, 1759, **1760, 1783**
  male milk, *iii*, 1758
  malformation, *iii*, 1759
  mammilla, *iii*, 1756, 1761, 1786
  mastitis, *iii*, 1761, **1764,** 1767
  mastodynia, *iii*, 1763
  micromastia, *iii*, 1759
  milk, *iii*, **1757**
  mixed tumors, *iii*, 1782
  Montgomery's glands, *iii*, 1759
  nipple, *iii*, 1756, 1761, 1787
  oidium albicans, *iii*, 1802
  Paget's disease, *iii*, 1787
  parametritis, *iii*, 1762
  parasites, *iii*, 1803
  pericanalicular fibroma, *iii*, 1777
  phlegmons, *iii*, 1762
  polymastia, *iii*, 1759
  polythelia, *iii*, 1759
  pregnancy, *iii*, 1759
  puerperal inflammation, *iii*, 1762
  retention cysts, *iii*, 1766, 1802
  sarcoma, *iii*, 1780, **1785, 1786**
  sarcoma phyloides, *iii*, **1781**
  and sex, *iii*, 1756
  syphilis, *iii*, 1770
  thelitis, *iii*, 1761
  thrush, *iii*, 1803
  trauma, *iii*, 1771, 1798
  tuberculosis, *iii*, 1768
  tumors, *iii*, **1771, 1786**
  witch's milk, *iii*, 1758
Bright's disease, *ii*, 1316
Bronchi, *i*, 337
  anatomy, *i*, 337
  arteries, *i*, 339
  asthma, *i*, 197, 344
  atelectasis, *i*, 355
  bacteria, *i*, 341, 347
  bronchiectasis, *i*, **351, 352, 354**
  broncholiths, *i*, 341, 355, 358
  bronchitis, *i*, 340, 343, 346, 404
  bronchopneumonia, *i*, **341, 342, 345**
  carcinoma, *i*, 351
  casts, *i*, **344**
  catarrh, *i*, 340
  cavities, *i*, 353
  circulation, *i*, 339
  congenital cysts, *i*, 356
  Curshman's spirals, *i*, 344, **345**
  cysts, *i*, 356
  dilatation, *i*, 351
  diphtheria, *i*, 343
  ectasia, *i*, 350
  eosinophilia, *i*, 346
  fetal bronchi, *i*, 338
  foreign bodies, *i*, 342, 356
  glanders, *i*, 340
Bronchi, glands, *i*, 350
  healing, *i*, 349
  influenza, *i*, 341
  lattice fibres, *i*, 339
  Leyden crystals, *i*, **345**
  lymph nodes, *i*, 259, 340, 342, 350, 358
  lymphatics, *i*, 340
  nerves, *i*, 345
  peribronchial focal pneumonia, *i*, 347
  spirals, *i*, 345
  stenosis, *i*, 350
  syphilis, *i*, 350
  toxemia, *i*, 341
  trauma, *i*, 358
  tuberculosis, *i*, 333, 343, **344, 345,** 348, **349,** 351
  tumors, *i*, 351, 358
  ulcers, *i*, 333, 337, 353
Bronchial glands, anthracotic, *i*, 340
  calculi, *i*, 358
  in asthma, *i*, 342
  tubercul., *i*, 259
Bronchiectasis, *i*, **351, 352, 354**
  atelectatic, *i* 355
Bronchioliths, *i*, 358
Bronchitis, *i*, 340
  catarrhal, *i*, 340
  chronic, *i*, 315
  Dittrick s plugs, *i*, 346
  fibrinous, *i*, 343
  putrid, *i*, 346
  tracheal, *i*, 312
Broncho-pneumonia, *i*, 342, 362, 401, 407
  passing into tuberculosis, *i*, 351
Brown, atrophy, heart, *i*, 49
    intestines, *i*, 804
    liver, *i*, 901
Bruit, aneurysmal, *i*, 134
Bubonic plague general, *i*, 252
    flea, *i*, 406
    pneumonic, *iii*, 2155
    spleen, *i*, 232
Bubo, *i*, 252
  bubonic plague, *i*, 252
  of soft chancre, *iii*, 2114
  suppuration, *iii*, 2114
Buhl's disease, *i*, 53
Bulbar paralysis, *iii*, 1993
Burns, death fr., *iii*, 2082
  duodenal ulcers, *iii*, 2082,
  in larynx, *i*, 313
  fr. lightning, *iii*, **2083**
Bursae, *iii*, 2065
  arthroma, *iii*, 2067
  carpal ganglion, *iii*, 2067
  gonorrhea, *iii*, 2065
  hemorrhage, *iii*, 2066
  hydrops, *iii*, 2065
  hygroma, *iii*, 2065, **2066**
  inflammation, *iii*, 2065
  prepatellar hygroma, *iii*, 2066
  rheumatism, *ii*, 1235, *iii*, 2065
  tuberculosis, *iii*, 2067
  tumors, *iii*, 2067

- CACHEXIA strumipriva, *i*, 527
- Caisson disease, *iii*, 2009
- Calcification, aneurysm., *i*, 135
  - aorta, *i*, 111
  - arteries, *i*, 102
  - endocardium, *iii*, 2341
  - heart, *i*, 23, 41, 54
  - kidneys, *iii*, 1308, 1331, 1378
  - lungs, *i*, 258, 285
  - lymph nodes, *i*, 258, 285
  - muscles, *iii*, 2039
  - peritoneum, *ii*, 870
  - thyroid, *i*, 521
  - veins, *i*, 161
- Calcium, *ii*, 1052, 1064, 1068, 1135, 1157
  - in ateriosclerosis, *i*, 103
  - in bone, *ii*, 1231
  - in rickets, *ii*, 1135
  - in syphilis, *ii*, 1135
- Calcium carbonate calculi, *ii*, 1412
- Calcium infarct of kidney, *ii*, 1378
- Calculi, in ampulla of Vater, *ii*, **998**
  - balanoliths, *ii*, 1540
  - biliary, *ii*, 982, 991, 1006
  - in bladder, *ii*, 1411, 1440, **1441, 1442**
  - bronchioliths, *i*, 358
  - calcium carb., *ii*, 1413
  - cholesterin, *ii*, 982
  - coproliths, *i*, 753
  - cystin, *ii*, 1412, 1441
  - enteroliths, *i*, 753
  - gall stones, *ii*, 982, 991
  - intestinal, *i*, 753
  - kidney, *i*, 304, *ii*, 1377, 1389, **1409, 1411, 1412**
  - oxalate, *ii*, 1381, 1412, 1440
  - pancreatic, *i*, **596**, *ii*, 1030, 1043
  - phleboliths, *i*, 155
  - phosphatic, *ii*, 1412, 1440
  - prepuce, *ii*, 1477, 1540
  - prostatic, *ii*, 1520
  - rhinoliths, *i*, 304
  - salivary, *i*, 596
  - seminal vesicles, *ii*, 1455, 1456, 1516
  - triple phosphate, *ii*, 1412
  - urate, *ii*, 1412, 1440
  - ureteral, *ii*, **1442**, 1456
  - urinary, *ii*, 1410, **1411, 1412**, 1424, **1441**,
  - veins, *i*, 155
  - xanthin, *ii*, 1413, 1441
- Callus, *ii*, 1055, 1085, 1177
  - callus cysts, *ii*, 1088
- Capillaries, *i*, 87, 97, **99**, 170
  - degeneration, *i*, 170
  - dilatation, *i*, 171
  - embolism, *i*, 171
  - hemorrhage, *i*, 171
  - inflammation, *i*, 170
  - of lymphatics, *i*, 172
  - stenosis, *i*, 171
  - thrombosis, *i*, 171
  - tumors, *i*, 108, 171, 172
- Caput medusae, *i*, 165
  - succedaneum, *ii*, 1193
- Carbon monoxide, *i*, 215
- Carbuncle, *iii*, 2106
  - of anthrax, *iii*, 2107
- Carcinoma of appendix, *i*, **816**, *ii*, **817**
  - basalcell, *i*, **182**, *iii*, **2202, 2203, 2204, 2205, 2206, 2207**
  - bladder, *ii*, 1423, 1424, **1435**, *iii*, 1697
  - in blood, *i*, 190
  - bone, *ii*, 1120, **1222, 1224**
  - bone marrow, *i*, 291
  - brain, *iii*, 1934
  - branchiogenic, *i*, 330
  - breast, *i*, 118, *iii*, 1763, 1768, **1783, 1785, 1786, 1788, 1789, 1791, 1792, 1793, 1794, 1795, 1796, 1797, 1800**
  - bronchi, *i*, 351, 385
  - cecum, *i*, **813**
  - cervix, *iii*, **1675**
  - cheek, *i*, 556, 572
  - chorioepithelioma, *iii*, 1698, 1717, **1740** to **1743**
  - coriocarcinoma, *i*, 181
  - esophagus, *i*, **640, 642, 644, 645, 647**
  - Fallopian tubes, *ii*, **1601**
  - finger, *iii*, **2212**
  - foot, *i*, **169**
  - gall bladder, *ii*, 1002, **1003**
  - gums, *ii*, 972
  - hand, *iii*, 2212
  - intestines, *i*, **696, 697, 811, 813, 814, 815, 816**, *ii*, **817, 818, 819, 820, 821, 823**
  - kidney, *ii*, 1389, 1391, 1400, **1401**
  - larynx, *i*, 322, **325**
  - leg, *i*, **169**
  - lips, *i*, 566, **567**
  - liver, *ii*, 893, **959, 960, 962, 966, 968**
  - lungs, *i*, 378, 470, **472, 474, 475, 478**
  - lymph nodes, *i*, **116**, 184, 282, **283**
  - lymph vessels, *i*, 175, 177, 179, 181
  - mouth, *i*, 556, 566, 568, **571**, 572, 592
  - nose, *i*, 304, *iii*, **2202**
  - ovary, *ii*, 1563, 1564, 1572, 1574, 1577
  - palate, *i*, **182**
  - pancreas, *ii*, **1046**
  - parotid, *i*, 593
  - penis, *ii*, 1538, **1539**
  - pericardium, *i*, 18
  - peritoneum, *ii*, 877
  - pharynx, *i*, 625, **626**, 634
  - pleura, *i*, 495
  - prostate, *ii*, **1529, 1530, 1531**
  - rectum, *iii*, 1697
  - salivary gland, *i*, 597
  - scalp, *iii*, **2220**
  - seminal vesicles, *ii*, 1415
  - spleen, *i*, 247, *iii*, **2201**
  - stomach, *i*, 687, 694, **695, 698, 700, 701, 703, 704, 705, 707, 708, 709**, 712
  - testicle, *ii*, **1498, 1499, 1500, 1501, 1502**
  - thoracic duct, *i*, 183
  - thyroid, *i*, 530
  - tongue, *i*, 566, **568, 569, 570**
  - tonsils, *i*, 625
  - urethra, *ii*, 1454
  - uterus, *iii*, **1673, 1674, 1675, 1678, 1680, 1684, 1685, 1686, 1687**

Carcinoma of vagina, *iii*, 167
  veins, *i*, 167
  vertebrae, *iii*, 2008
  vulva, *iii*, **2201**
Cardia, *i*, 715
Cardiospasm, *i*, 650
Caries of bone, *ii*, 1103, **1130, 1138**
  joint, *ii*, 1231
  syphilitic, *ii*, 1139
  teeth, *i*, 576
Carnification of lung, *i*, 399
Carotid gland, *i*, 330
Carriers of infection, polyomyelitis, *iii*, 1991
  typhoid, *i*, 783, *ii*, 1001
Cartilage, *ii*, 1062, 1229
  anlage, *ii*, 1172
  arytenoid, *i*, 305
  changes in, *ii*, 1232
  chondrodystrophy, *ii*, 1170
  cricoid, *i*, 314
  degeneration, *ii*, 1229
  ecchondrosis, *ii*, 1196
  enchondromas, *ii*, 1194, 1203
  gigantism, *ii*, 1150
  growth, *ii*, 1158
  joint mice, *ii*, 1274
  joints, *ii*, 1150
  larynx, *i*, 305
  metaplasia, *ii*, 1155
  osteochondritis, *ii*, 1274
  osteoidchondromas, *ii*, 1206
  perichondrium, *ii*, 1149
  replacement, *ii*, 1148
  Santorini's, *i*, 305
  trachea, *i*, 305
  tumors, *ii*, 1194
  Wrisberg's, *i*, 305
Caruncles, urethral, *ii*, 1453
Caseation lung, *i*, 408, 437
  lymph glands, *i*, 257
Castration, *ii*, 1186, 1702
Casts, bronchial, *i*, **344**
  renal, *ii*, **1326**
  urinary, *ii*, 1326, 1327
Catarrh, *i*, 34
  bronchial, *i*, 340
  esophagus, *i*, 634
  gastric, *i*, 665
  intestinal, *i*, 760
  larynx, *i*, 308, 310
  nose, *i*, 293
  pharynx, *i*, 617
  smokers, *i*, 310
  stomach, *i*, 665
  vagina, *iii*, 1692
Cavities in bone, *ii*, 1133
  bronchial, *i*, 353
  joints, *ii*, 1229
  lungs, *i*, 446, **448, 453**
  lymph vessels, *i*, 175
  metamorph. cavernous of veins, *i*, **154**
Cecum, *i*, 720, *ii*, 831
  carcinoma, *i*, **813**
  pericecal hernia, *i*, 737
  tuberculosis, *i*, **800**
Cells, *i*, 200
  Altmann granules, *i*, 194, 196
  ameboid glia cells, *iii*, 1877
  basophiles, *i*, 185
  basophilic degeneration, *i*, 188
  blood platelets, *i*, 286
  bone marrow cells, *i*, 286
  cell pictures, *i*, **200**
  chorionic cells, *iii*, 1716
  chromaffin cells, *ii*, 1276, 1289
  chromaphile cells, *iii*, 1946
  chromatophores, *iii*, 1843
  clasmatocytes, *i*, 10, *iii*, 1875
  connective tissue cells, *i*, 9, 10
  Ehrlich-granules, *i*, 194, 196
  elastoblasts, *i*, 89, 188
  eosinophiles, *i*, 10, 197, 346, *iii*, 2040
  erythroblasts, *i*, 188, 287
  erythrocytes, *i*, 185, 187
  fat granule cells, *iii*, 1871, 1901
  ganglion cells, *iii*, 1872, 1878
  genital cells, *ii*, 1460
  giant cells, *i*, 10, 11, 180, 263, 268, 286, 423, **573**, *ii*, 1215, 1623, *iii*, 1712, 1717, 1745
  histiocytes, *i*, 219
  Howell-Jolly bodies, *i*, 188
  interstitial cells, *ii*, 1479
  Kupfers cells, *ii*, 1017
  Langhans giant cells, *i*, 10, *iii*, 1712, 1745
  lattice cells, *iii*, 1867
  leucocytes, *i*, 10, 187, 194, **200**, 221
  liver cells, *ii*, **903**
  lutein cells, *ii*, 1448
  lymphoblasts, *i*, 194
  lymphocytes, *i*, 10, 194, 198, **200**
  macrocytes, *i*, 188
  macrophages, *i*, 10, 187, 221
  marrow cells, *i*, 187, 195, 198
  mast cells, *i*, 10, 195
  megacaryocytes, *i*, 187, 286
  megaloblasts, *i*, 189, 190, **192**, 287
  microcytes, *i*, 188
  Mikulicz cells, *i*, 300
  mitosis, *i*, 201
  monocytes, *i*, 196
  myeloblasts, *i*, 195, 202, 286
  myeloclasts, *iii*, 2034
  myelocytes, *i*, 190, 198, 286
  myeloplaxes, *i*, 286, *iii*, 2064
  nerve cells, *iii*, **1871**
  neurocytes hydrophobiae, *iii*, 1900
  neuronophagia, *iii*, 1872
  normoblasts, *i*, 189, 286
  odontoblasts, *i*, 585
  osteoblasts, *i*, 286, *ii*, 1056
  osteoclasts, *ii*, 1056
  ovarian cells, *ii*, 1568
  oxidase reaction, *i*, 196
  in pericarditis, *i*, 9
  perithelial cells, *i*, 178
  phagocytes, *i*, 219, *iii*, 1875
  pigment granule cells, *i*, 217, *iii*, 1874
  plasma cells, *i*, 9, 268, 272, **309**, *iii*, 1867
  plasmocytes, *i*, 9
  poikilocytes, *i*, **192, 200**

- Cells, polymorphonuclear neutrophiles, *i*, 10
  - Purkinjè's cells, *iii*, 1878
  - pyknosis, *iii*, 1871
  - pyrrhol cells, *i*, 10
  - Sertoli's cells, *ii*, 1480
  - sickle cells, *i*, 193
  - Sternberg's giant cells, *i*, 268
  - stipple cells, *i*, 188
  - sympathoblasts, *ii*, 1288
  - thrombocytes, *i*, 186
  - tigroid cells, *iii*, 1872
  - tumor cells in blood stream, *i*, 190
  - tumor cells in lymphatics, *i*, 185
  - wandering cells, *i*, 9
  - xanthoma cells, *iii*, 2064
- Cephal hematoma, *ii*, 1093
- Cercomonas, *ii*, **849**, 857
- Cerebrospinal fluid, *iii*, 1805, 1846
- Cerebrospinal meningitis, *iii*, 1830
- Cervical lymph nodes, *i*, 258
- Cervix uteri, *ii*, 1631
  - carcinoma, *iii*, **1673, 1674, 1675, 1676**
  - ectropion, *ii*, 1631, *iii*, 1643
  - elongation, *iii*, 1643
  - erosion, *ii*, 1631, *iii*, **1635**
  - gonorrhea, *ii*, 1631
  - syphilis, *iii*, 1641
  - tuberculosis, *iii*, 1640
- Cestodes, *ii*, 847
- Chaga's disease, *i*, 212
- Chalicosis, *i*, 421
- Chancroid, soft chancre, *i*, 252, *ii*, 1454, 1534
- Charcot's crystals, *i*, 204, 268, 346
- Charcot's disease, *iii*, 1962
- Charcot's joint, *ii*, **1251**
- Cheilachisis, *i*, 545
- Cheilitis, *i*, 548
- Chest, chicken breast, *ii*, 1163
  - funnelchest-pigeonbreast, *ii*, 1163
  - emphysema, *i*, **367**
- Chilblain, *iii*, 2071
- Children incl. newborn, diseases, atresia anal, *i*, 722, **723**
  - atresia esoph., *i*, 632
  - Barlow's infantile scurvy, *ii*, 1166
  - birth traumas, *iii*, 1810, 1811, 1823, 1849, 1860
  - births, late, *ii*, 1187
  - blue baby, *i*, **91**
  - Buhl's disease, fatty cord. deg. w. cyanosis in newborn, *i*, 53
  - carcinoma kidney, *ii*, 1389, **1408**
  - cephalhematoma, *iii*, 1810
  - chloroma, *i*, 274
  - cretinism, *i*, 523, *ii*, **1182, 1185**
  - cyanosis congenit., *i*, 44
  - diphtheria, *i*, 294
  - epidermolysis, *iii*, 2089
  - fontanelles, *ii*, 1084, 1164
  - giantism, *ii*, 1187
  - gonorrhea, *ii*, 1453, *iii*, 1693
  - harelip, *i*, 545
  - hemiplegia spastica, *iii*, 1869
  - hemorrhag. infarct kidney, *ii*, 1307
- Children incl. newborn, diseases, atresia anal, hereditary ataxia (Friedreichs dis.), *iii*, 2005
  - hermaphroditism, *ii*, 1466, **1481, 1483**
  - Hirschsprung's dis. dilat. colon in boys, *i*, 720, **721**, 736
  - hydrocephalus, *iii*, 1823, 1832
  - ichthyosis, *iii*, **2171**
  - icterus neonat, *ii*, 1017, *iii*, 2038
  - lactation, *iii*, **1758**
  - Little's dis. infantile spasm. tabes, *iii*, 1997
  - malformations, *ii*, 1169
  - mastitis, *iii*, 1761
  - Medin's dis. ac. ant. poliomyelitis in children, *iii*, 1990
  - meningitis suppur, *iii*, 1829
  - mongolianism, *i*, 526
  - myxedema, *i*, 529
  - nannosomia, *ii*, 1179
  - nasal diphth., *i*, 294
  - noma, *i*, **552**
  - ophthalmia neonat., *ii*, 1453
  - ovarian tumors, *ii*, **1575**
  - pemphigus, *iii*, 2088
  - poliomyelitis ac. anterior, *iii*, 1990
  - precocity (sex.), *iii*, 1958
  - pyloric stenosis congenit. *i*, 660, 713
  - scleroderma, *iii*, 2170
  - scrofulosis, *i*, 242, 260
  - sex-precocity, *iii*, 1958
  - skull fissures, *ii*, 1084, 1164
  - smallpox, *iii*, **2093, 2094**
  - spinal hemorrh. in newborn, *iii*, 1961
  - stenosis of aorta, cong., *i*, 28, 47
  - stenosis of intestines, congen., *i*, 720
  - syphilis, cong., *i*, 131
  - thrombosis renal vein, *ii*, 1300
  - torticollis, *iii*, 2046
  - tubercul. of lymph nodes, *i*, 256, 260
  - tubercul. meningitis, *iii*, 1832, 1833, 1834
  - tubercul. pulmon. *i*, 458
  - Werlhoff's purpura neonat., *i*, 509, *iii*, 2073
  - Winkel's fatty degen. of heart in newborn, *i*, 53
  - wry neck, *iii*, 2046
- Chloroma, *ii*, 1221
  - of lymph glands, *i*, 272, 274
  - myeloid chloroma, *i*, **273**
- Chlorosis, *i*, 187, 189
- Cholangitis, *ii*, 981
- Cholecystitis, *ii*, 984, 1029
- Cholelithiasis, *ii*, 983
  - calculi, *ii*, 982, **998**
  - colon bacilli, *ii*, 981, 1001
- Cholera, *i*, 777
  - and arsenical poisoning, *i*, 781
  - bacilli, *i*, 777
  - kidney, *ii*, 1302, 1316
- Cholesteatoma, *iii*, **1840**
- Chondrodystrophy, *ii*, **1173**
  - pelvis, *ii*, 1175

Heavy face type denotes an illustration.

- Chondroma, *ii*, 1201
  - chondromatosis, *ii*, 1275
  - metastatic, *i*, 167
- Chorion, *iii*, 1711
  - cell layer of Langerhans, *iii*, 1712, 1745
  - chorionic villi, *iii*, 1716
  - placenta, *iii*, 1710, 1711, 1715, 1720
  - syncytium, *iii*, 1712, 1724
- Chorion-epithelioma malignum, *iii*, 1717, 1722, 1727, **1740, 1741, 1742, 1743**
  - metastasis, *iii*, 1935
  - in lung, **477**
  - regression of metastasis, *iii*, 1745, 1746
  - of testes, *ii*, **1507, 1508** *iii*, 1746
  - of vagina, *iii*, 1744
- Choroideal tubercle, *i*, 432
- Chrobak's pelvis, *ii*, 1266
- Chromaffin cells, *ii*, 1277, 1289
  - hyperplasia, *i*, 500
- Chromatophores, *iii*, 1843
- Chrysops discalis; horsefly, *i*, 262
- Chylothorax, *i*, 176
- Chylous ascites, *i*, 176
- Chyluria, *i*, 210
- Chylus, cysts, *i*, 177
  - system, *i*, 172
  - tuberculosis, *i*, 174
- Chyme, *i*, 751
- Cimex lect. (bed bug), *iii*, 2155
- Circulation disturb. arteries, *i*, 97
  - blood, *i*, 185, 216, 286
  - bronchi, *i*, 339
  - capillaries, *i*, 97
  - esophagus, *i*, 632
  - heart, *i*, 1
  - intestines, *i*, 718
  - joints, *ii*, 1233
  - kidneys, *ii*, 1293, 1299, 1302
  - larynx, *i*, 305
  - liver, *ii*, **880,** 890
  - lungs, *i*, 370, 380
  - lymph, *i*, 172
  - lymph glands, *i*, 249
  - nose, *i*, 292
  - ovaries, *ii*, 1547
  - pancreas, *ii*, 1022
  - peritoneum, *ii*, 862, 880
  - pharynx, *i*, 605
  - spleen, *i*, 218, 223, *ii*, **880**
  - stomach, *i*, 661
  - thyroid, *i*, 508
  - uterus, *ii*, 1617
  - veins, *i*, 152
- Cirrhosis, biliary, *i*, 225, *ii*, 921, **922, 923, 924, 925, 926**
  - cirrhosis of liver and hemoptysis, *i*, 633
  - Hanot's, *ii*, 929
  - kidneys, *ii*, 1314
  - Laennec's, *i*, 225, *ii*, 921, **927**
  - pancreas, *ii*, 1029
- Clavus (corns), *iii*, 2166
- Clitoris, *iii*, 1701, 1702, 1705, 1706
- Cloaca, *i*, 722, *ii*, 1424
- Coagula in heart, *i*, 58, 72, 81
- Coccidium, *ii*, 883
- Coccygeal gland, *i*, 331
- Cold, (catching a cold), *i*, 294, 404
- Colitis, *i*, 766, *ii*, 831
- Collapse of lungs, *i*, 359, 362
- Coloboma, *i*, 545
- Colon, carcinoma, *ii*, **821**
  - colitis, *i*, **766,** *ii*, 831
  - dilatation, *ii*, 821
  - dysentery, *i*, 768
  - Hirschsprung's disease, *i*, 721
  - lipoma, *i*, **807**
  - polyposis, *i*, **811, 812**
  - tumors, *ii*, 820
- Colostrum, *iii*, 1758
- Colpitis, *iii*, 1692
- Comedo (demodex), *iii*, 1803, 2156, 2217
- Condyloma, *ii*, **1537,** *iii*, 1696, 1704, 1705
  - condyloma lata, *iii*, 2136
- Congenital defects, aneurysm, *i*, 150
  - bladder, *ii*, 1422
  - brain, *i*, 142, *iii*, 1807, **1883, 1885, 1887**
  - branchiogenic, *i*, 327
  - esophagus, *i*, 630
  - heart, *i*, 1, 28, 47, 86, 89
  - intestines, *i*, 719
  - kidney, *ii*, 1296
  - larynx, *i*, 306
  - lungs, *i*, 359
  - mouth, *i*, 544
  - nose, *i*, 292
  - pancreas, *ii*, 1021
  - sex organs, *ii*, 1466, **1481, 1483**
  - skull, *ii*, 1189
  - spleen, *i*, 220
  - stenosis of aorta, *i*, 28, 47
  - stenosis pylorus, *i*, 660, 713
  - thyroid, *i*, 506
  - tumors, *ii*, 1391
  - ureters, *ii*, 1296
  - urethra, *ii*, 1424, 1448
- Conjunctivitis, *ii*, 1453
- Conorhinus, *i*, 212
- Constipation, *i*, 751, *ii*, 845
- Consumption, galloping, *i*, 429
- Conus pulmonalis, *i*, 92, 97
- Copper line, *i*, 550
- Coproliths, *i*, 753
- Coprostasis, *i*, 751
- Cor villosum, *i*, 7
- Cord, umbilical, *iii*, 1733
- Cord, vocal, *i*, 305, 310
- Cords, spermatic, *ii*, 1415, 1476, 1484, 1511
  - tuberculosis, *ii*, 1415
  - tumors, *ii*, 1415
- Coriocarcinoma, *i*, 181
- Corns (clavus), *iii*, **2166**
- Coronary arteries and veins, *i*, 4, 55, 56, 107, 125
- Corpora libra, joint mice, *ii*, 1273
  - ricebodies, *ii*, 1275
- Corpus luteum, *ii*, **1543**
  - adenoma, *ii*, **1575**
  - cysts, *ii*, 1552, **1560**
  - of pregnancy, *ii*, 1618
- Coryza, *i*, 293

Heavy face type denotes an illustration.

- Cotyledons, *iii*, 1714, 1722
- Cowper's glands, *ii*, 1457
- Coxa valga, *ii*, 1072
  - vara, *ii*, 1072, 1166, 1272
- Coxitis, *ii*, 1132, 1268
- Craniotabes, *ii*, 1156, 1165
- Cretinism, *i*, 523, *ii*, 1183
  - athyreosis, *ii*, 1181, **1182**
  - dwarf, *ii*, 1182
  - goiter, *ii*, 1181
  - skeleton, *ii*, **1185**
- Cricoid cartilage, *i*, 314
- Croup, *i*, 311
  - pseudomembranous, *i*, **332**
- Cryptorchism, *ii*, 1476
- Curschmann's spirals, *i*, 344
- Cyanosis-congenit., *i*, 44
  - cardiac, *i*, 44, 53, 55, 56
- Cyclops, *i*, **547**
- Cylindroma, *i*, 182
- Cynanche, *i*, 596
- Cystadenoma, ovar., *ii*, **1556, 1558, 1589, 1560, 1563**
- Cysticercus, *i*, 285, 576, *ii*, 848, 1402, *iii*, 1845, 1852, 1939, **2060**
- Cystin calculi, *ii*, 1412
- Cystitis, *ii*, 1426
- Cystocele, *ii*, 1427
- Cystoids, *ii*, 1049
- Cystoma, ovarian, *ii*, **1560, 1561, 1562**
- Cystpapilloma mal. thyroid, *i*, 534
- Cysts, adrenal, *ii*, **1282,** 1289
  - bone, *ii*, **1226**
  - branchiogenetic, *i*, 327
  - of broad ligament, *ii*, 1554
  - bronchial, *i*, 356
  - callus cysts, *ii*, 1084, 1088
  - chylus cysts, *i*, 177
  - dental cysts, *i*, 586
  - dermoid cysts, *ii*, 1583
  - echinococcus cysts, *ii*, 971
  - eosophagus, *i*, 638
  - hydatid cysts, *iii*, 1695
  - hydatids of Morgagni, *ii*, 1464
  - intestinal, *i*, 727, 764
  - kidney, *ii*, 1311, 1318, **1382, 1383, 1386**
  - laryngeal, *i*, 306
  - liver, *ii*, 955, **956, 972, 974, 975**
  - lymphatics, *i*, 177
  - mouth, *i*, 574, 575
  - oil cysts, *iii*, 2178
  - ovarian, *ii*, 1552, **1560, 1562, 1563**
  - pancreas, *ii*, 1021, 1027, **1048, 1049,** 1384
  - penis, *iii*, 2178
  - peridontal, *i*, 588
  - peritoneum, *ii*, 874
  - root cysts, *i*, 586
  - spleen, *i*, 246
  - teeth, *i*, 586
  - testicle, *ii*, 1494
  - thyroid, *i*, 520
  - tongue, *i*, 507, 574
  - tubes (fallop.), *ii*, 1464
  - tubo-ovarian, *iii*, 2187

- Darrier's disease, psorospermosis, *iii*, 2157
- Death, *i*, 155
  - from air embolism, *i*, 207
  - aneurysm-rupture, *i*, 143
  - asphyxia, *i*, 293, 383
  - from burns, *iii*, 2082
  - cardiac, *i*, 62
  - coronary art. occlus, *i*, 55
  - drowning, *i*, 413
  - from fatty heart, *i*, 54
  - hanging, *i*, 71
  - newborn, *i*, 293
  - pulmon. art. embolism, *i*, 46
  - status lymphaticus, *i*, 499
  - sudden death, *i*, 155
  - thymus death, *i*, 500
  - thymus glands and suicide, *i*, 501
- Deciduae, *iii*, 1708
  - endometritis, *ii*, 1623
  - membranes, *iii*, 1710, 1718
  - menstrual, *ii*, 1618
  - pregnancy, *iii*, 1708
  - villi, *iii*, 1712
- Decubital necrosis with intubation, *i*, 337
- Decubital ulcers—bronchi, *i*, 337
  - intestinal, *i*, 485
  - pharynx, *i*, 627, **628**
  - of skin, *iii*, 2108
- Deficiency diseases, beri-beri, *i*, 216
    - pellagra, *iii*, 2002
    - rachitis, *ii*, 1151
    - scurvy, *i*, 550, *iii*, 2073
    - scurvy-infantile, *ii*, 1166, *iii*, 2074
- Degenerations, of adrenals, *ii*, 1286
  - albuminous, *ii*, 1318, 1329
  - amyloid, *i*, 23, 25, 55, 106, 107, 110, **243, 244,** 285, 522, 758, 805, *ii*, 905, 1038, 1286, 1358, 1359
  - of arteries, *i*, 101, 102, 106, 107, 110
  - atheromatous d., *i*, 20, 23, 110
  - basophilic d. erythrocytes, *i*, 188, 551
  - capillaries, *i*, 170
  - cystic d. papillae of tongue, *i*, **563**
  - fatty, d., *i*, 22, 51, 61, 101, 285, *ii*, 902, 1301, **1320**
  - goiter, *i*, 521
  - heart, *i*, 20, 22, 23, 51, 55, 61
  - hyalin d., *i*, 23, 106, 285, 521, *ii*, 1322, **1323**
  - hydropic, *ii*, 1323, *iii*, **2037**
  - intestines, *i*, 758, 804
  - joints, *ii*, 1243
  - kidney, *ii*, 1301, 1315, 1317, 1318, 1319, **1320,** 1322, **1323,** 1329, 1358, **1359**
  - liver, *ii*, 902, 905
  - lymph glands, *i*, 285
  - muscles, *iii*, **2037**
  - pancreas, *ii*, 1038
  - spleen, **243, 244**
  - stomach, *i*, 712
  - thyroid, *i*, 521
  - tongue-papillae, *i*, **563**
  - vessels, *i*, 101, 106, 110
  - waxy d., *iii*, **2037**
- Dementia paralytica, *iii*, 1864

Heavy face type denotes an illustration.

- Demodex follic. (comedo), *iii*, 2155, 2217
  - breast, *iii*, 1803
- Dental osteoma, *i*, 586
- Dental tartar, *i*, 580
- Dentine, *i*, 578, *i*, 585
- Dercum's dis. (adiposis dolorosa), *iii*, 2179
- Dermacentor andersoni stiles, *i*, 262
- Dermatitis exfol., *iii*, 2074, 2075
- Dermatomyeosis, *iii*, 2148
- Dermatozoa, *iii*, 2155
- Dermoid cysts and dermoids, dermoid-atheroma, *iii*, **2218**
  - mouth, *i*, 575
  - ovary, *ii*, 1568, 1582
  - testes, *ii*, 1503
- Diabetes insipidus, *iii*, 1949
- Diabetes mellitus, *ii*, 1322
  - furunculosis, *iii*, 2105
  - gangrene, *i*, **104, 105,** 106
  - kidney, *ii*, 1322, 1324
  - liver, *ii*, 949
  - pancreas, *ii*, 1036
  - spleen, *i*, 237, *ii*, 1035
  - xanthosis, *iii*, 2161
- Diabetic puncture, *ii*, 1278
- Diaphragm, *i*, 172
  - hernia, *i*, 359, 737
  - pelvic, *ii*, 1614
  - sarcoma metast., *iii*, 1665
  - thoracic duct, *i*, 172
- Diaphysis, *ii*, **1117,** 1152, **1158,** 1171
- Diarrhea, *i*, 761, 763
- Diarthroses, *ii*, 1228
- Diastole, *i*, 46
- Diphtheria, bacilli, *i*, 312, 560, 608, 611
  - bronchi, *i*, 343
  - esophagus, *i*, 636
  - heart, *i*, 61, 65
  - intestines, *i*, 768, 774
  - kidney, *ii*, 1316, 1329, 1338, 1364
  - larynx, *i*, 311, 319
  - mouth, *i*, 560
  - nose, *i*, 294
  - palate, *i*, 608
  - pharynx, *i*, 607, **611**
  - predisposition, *i*, 609
  - pseudomembrane, *i*, 610
  - sequelae, *i*, 613
  - stains, *i*, 608, 611
  - tonsils, *i*, 609
  - vulva, *iii*, 1702
- Diplococcus intracell. mening., *iii*, 2030
- Diplococcus lanc. pneum., *i*, 394
- Diploe, *i*, 158
- Diseases, Addison's (adrenal), *ii*, 1279, 1283
  - Alzheimer's (mental), *iii*, 1862
  - Banti's (spleen), *i*, 224
  - Basedow's (thyroid), *i*, 501, 516
  - Bright's (kidneys), *ii*, 1316
  - Buhl's (fatty deg. heart new-born with cyanosis, *i*, 53
  - Chaga's, Brazilian trypanosomiasis, *i*, 212
  - Charcot's multiple sclerosis, *iii*, 1962
  - Darier's pseudospermosis, *iii*, 2157
  - Dercum's adiposis dolor., *iii*, 2175
  - Friedreich's heredit. ataxia, *iii*, 2005
  - Grave's (thyroid), *i*, 501
  - Heine-Medin's ac. ant. poliomyel. children, *iii*, 1990
  - Hirschsprung's dilat. colon boys, *i*, 720, 736
  - Hodgkin's lymphogranuloma, *i*, 193, 266, 271
  - Little's infant. spasm. tabes, *iii*, 1997
  - Mikulicz's chr. enlargem. of lacrym. and saliv. glands, *i*, 604
  - Moller-Barlow's infant. scurvy, *ii*, 1166, *iii*, 2074
  - Morvan's dis. spin. cord, *iii*, 1981
  - O'hara's japan. tularemia, *i*, 262
  - Paget's disease of bone, *ii*, 1107
  - Paget's dis. of nipple, *iii*, 1787, 2211
  - Parkinson's paralys. agit., *i*, 542, *iii*, 1913
  - Pott's tuberc. vertebrae, *ii*, 1130, 1267
  - Raynaud's sym. gangr. fingers etc., *iii*, 2110, 2147
  - Recklinghausen's neurofibromatosis, *iii*, **2027**
  - Thomsen's myotonia, *iii*, 2049
  - Vaques-Osler's erythremia, 188
  - Weil's infect. icterus, *i*, 214, *ii*, 1019
  - Werlhoff's purpura hem., *iii*, 2073
  - Wilson's progr. deg. lentic. nucleus, *ii*, 954, *iii*, 1863
  - Winkel's fatty card. deg. new-born, *i*, 53
- Dislocation of bone, *ii*, 1090
  - of joints, *ii*, 1086, 1090
- Distention of intestines, *i*, 750
  - lungs, *i*, 363
- Distomum hemat., *i*, 211
  - bladder, *ii*, 1447
  - intestines, *i*, 856
  - kidney, *ii*, 1402
  - liver, *ii*, 972
  - lungs, *i*, 481
- Dittrich's plugs, *i*, 346
- Diverticuli of bladder, *ii*, **1444, 1445**
  - esophagus, *i*, 652
  - fallop. tubes, *ii*, 1592
  - intestinal, *i*, 725, 749
  - Meckel's, *i*, 725, 748
  - pharynx, *i*, 629
  - pulsion, 653
  - stomach, *i*, 716
  - traction, *i*, 652
- Dolichocephalia, *ii*, 1189
- Douglas's cul de sac, *ii*, 883, 1549, 1612
- Dropsy, *i*, 308
- Drowning, *i*, 413
- Drug-exanthemata, *iii*, 2081
- Drumstick fingers, *ii*, 1082
- Ducts, Bartholin's, *i*, 575
  - bile, *ii*, 979
  - Bochdalec's in root of tongue, *i*, 507, 574
  - Botalli's duct. art., *i*, 95, 97
  - Gartner's (prim. kidney), *ii*, 1459, 1464
  - lingual, *i*, 575
  - Luschka's in G. B., *ii*, 979, 997
  - Müllers' (prim. kid.), *ii*, **1458,** 1460, 1462, 1464

Heavy face type denotes an illustration.

Ducts, pancreatic, *ii*, 1021
  Santorini's (pancr.), *ii*, 1021
  Stenson's parotid, *i*, 593
  thoracic, *i*, 172, 176, 482
  Wirsung's (pancr.), *ii*, 1021
  Wolffian prim. kidney, *ii*, **1458**
Duodenum, *i*, 718, *ii*, 829
Dura mater, hematoma, *iii*, **1813**
    hygroma, *iii*, **1814**
    psammoma, *iii*, **1817**
    psammosarcoma, *iii*, **1820, 1821**
    sarcoma, *i*, 172, *iii*, **1822**
    tuberculosis, *ii*, 1131
Dwarfism, *ii*, 1179
  chondrodystrophic, *ii*, 1174
  cretinism, *i*, 523, *ii*, 1182
  myxedematous, *i*, 529
  nannosomia, *ii*, 1179
  Paltauf's, *ii*, 1180
  pituitary, *ii*, 1180
  rachitic, *ii*, 1163
Dysentery, *i*, 770, 772
  arthritides, *ii*, 1237
Dysmenorrhea, *iii*, 1737
Dysostosis, *ii*, 1198
Dyspnea, hemoglobin, *i*, 189
Dystopia, renal, *ii*, 1295
Dystrophy, and kidney, *ii*, **1295,** 1318

Ear, *i*, 295, 614, *iii*, 1826
  otitis media, *iii*, **1826**
Ecchondrosis, *ii*, 1196
Echinococcus, adrenal, *ii*, 1291
  in bone, *ii*, 1227
  brain, *ii*, 938
  heart, *i*, 86
  kidney, *ii*, 1402
  liver, *ii*, 971, **972, 974, 975**
  lungs, *i*, 481
  lymph glands, *i*, 285
  mediastinum, *i*, 505
  mouth, *i*, 576
  ovary, *ii*, 1589
  peritoneum, *ii*, 883
  spinal canal, *ii*, 963
  spleen, *i*, **247,** 254
  testes, *ii*, 1510
  thyroid, *i*, 537
Eclampsia, *i*, 162, *iii*, 1717
  kidney, *ii*, 1302, 1310, *iii*, 1727
  liver, *ii*, **897**
  vessels, *i*, 151
Ectopic gestation, *ii*, 1603, 1606, 1609, **1610** *iii*, 1710, 1737
  ovary, *ii*, 1619
  tubal, *ii*, 1603
Ectropion uteri, *ii*, 1631, *iii*, 1643
Eczema, eosinoph., *i*, 197, *iii*, 2098, 2090
Edema of glottis, *i*, **307**
  intestinal, *i*, 755
  larynx, *i*, 307, 615
  liver, *ii*, 900
  lung, *i*, 374, 377
  scrotum, *ii*, 1533
  skin, *ii*, 1341
Edema of vulva, *iii*, 1701
Elbow, *ii*, 1272, **1274**
Elephantiasis, *i*, **176,** 211
  acquired, *iii*, 2112
  eyelid, *iii*, **2025**
  filaria, *i*, 211
  lymphangiectatic, *i*, 177, *iii*, **2169**
  neuroma, *iii*, 2026
  phlebectatic, *i*, 167
  vulva, *i*, 176
Embolism, *i*, 116, 152, 155
  aneurysm, *i*, 147
  capillaries, *i*, 171
  fat embolism, *i*, 207, **387**
  heart, *i*, 36, 41, 48
  intestinal, *i*, 735, 756
  kidney, *ii*, 1303, 1306, 1310
  lung, *i*, 155, 381, **383,** 388, 413
  pulmon. art., *i*, **383**
  recanalization, *i*, 121
  retinal artery, *i*, **119**
  splenic art., *i*, 226
  veins, *i*, 155
Embryo, *ii*, **1458, 1465,** 1621
  blood, *i*, 198
  heart, *i*, **87**
  intestines, *i*, 722
  testes, *iii*, **1781**
  uterus, *ii*, **1471**
Emphysema, *i*, 363
  intestines, *i*, 765
  lung, *i*, 363, 398
  pleura, *i*, 485
Empyema antrum, *i*, 296, 579
  gall bladder, *ii*, 1000
  joint, *ii*, 1235
  pleura, *i*, 487
Enamel, *i*, 576, 580
  adamantoma, *i*, **589, 590**
  enamel plug granuloma, *i*, **591**
Encephalitis, chronic, *iii*, 1907
  lethargic, *iii*, 1900
  neonatorum, *iii*, 1901
  suppuration, *iii*, 1902
Encephalomalacia, *i*, 116
Enchondroma, *i*, 184, *ii*, 1194, 1198, 1202, 1205
Endarteritis, *i*, 117
  brain, *i*, **130**
  obliterans, *i*, 120, **130**
  productive, *i*, 117
Endocarditis, actinomycosis, *i*, 17
  acute, *i*, 25–35, **27, 29, 31, 32, 40**
  amyloid, *i*, 41
  aneurysm aorta, *i*, 32
  annulus fibrosus, *i*, 41
  aorta, *i*, 45
  aortic veget., *i*, 33
  autopsy findings, *i*, 38, 72, 81
  bacteria, *i*, 15, 26, 28, 31, 33, 35, 37, 38
  calcification, *i*, 23, 41
  cardiac chambers, *i*, 47
  chronic, *i*, 28, 39
  congenital cyanosis, *i*, 44, 48
  embolism, *i*, 36, 41, 48

Endocarditis, endocarditis lenta, *i*, 33
  fibrous e., *i*, 27, 38
  gonorrheal, *i*, **34,** 35
  heart failure, *i*, 42
  heart lesions, congenit., *i*, 28, 47
  insufficiency, *i*, 46
  kidneys, *i*, 38
  leaflets fused, *i*, 39
  mitral insuff., *i*, **40,** 44
  mitral stenosis, *i*, 43
  mycotic. e., *i*, 33
  in newborn, *i*, 30, 53
  noduli albini, *i*, 28
  Osler's nodes, *i*, 38
  ossification, *i*, 39
  parietal e., *i*, 32, 33
  perforation, *i*, 31
  petrification, *i*, 39
  productive e., *i*, 27
  pulmon. valves, *i*, 46
  recurrent, *i*, 28, 40
  sinus of Valsalva, *i*, 33
  stenosis, *i*, **40,** 42, 45
  streptococcus viridans, *i*, 33
  thrombosis, *i*, 26, **79**
  toxins, *i*, 26
  tricuspid, *i*, 46
  tuberculosis, *i*, 47
  ulcerative e., *i*, 28, 30, **31,** 35
  valve lesions, *i*, 42, 43, 46, 47
  valvul. e., *i*, 25, 39
  vegetat. e., *i*, 28, 29, 35
  verucose e., *i*, **27, 29**
Endocardium, *i*, 19, **27, 29, 31, 32**
  Adam-Stokes symptom complex, *i*, 21
  amyloid deg., *i*, 23
  atheromat. degen., *i*, 23
  atrioventric system, *i*, 20
  auricles, *i*, 21
  bacteria, *i*, 36, 37
  bundle of His, *i*, 20, 21, 22
  calcification, *i*, 23, **24**
  degenerations, *i*, 22, 23
  diagnosis, *i*, 25
  endocarditis, *i*, 25
  fatty degen., *i*, 22
  heartblock, *i*, 21
  hemorrhage, *i*, 21
  hyalin deg., *i*, 23
  nerves, *i*, 20
  poisons, *i*, 52, 53
  Purkinje's fibres, *i*, 19
  sclerosis, *i*, 23, **24**
  softening, *i*, 23
  Tawara's conducting system, *i*, 19
  ventricles, *i*, 21
  vessels of valve leaflets *i* 22
Endocrine relations, *i*, 528
Endometritis, *ii*, 1623, *iii*, 1718, 1751
  hyperplasia, *ii*, **1626**
  malign. adenoma, *iii*, **1682**
Endosteum, *ii*, 1057, **1058,** 1152
Endothelioma, *i*, 180, 187
  blood vessels, *i*, 179
  brain, *i*, 181

Endothelioma, dura, *i*, 181, *iii*, 1963
  endothelial carcinoma, *i*, 175
  endothelial psammoma, *i*, 181
  endothelial sarcoma, *i*, 179
  lymphangiomatosis, *i*, 178, **180**
  ovaries, *i*, 181
  palate, *i*, **182**
  peritoneum, *ii*, **876**
  pleura, *i*, 493
Enteritis, *i*, 758, 763, 767, 771
Enterokinase, *ii*, 1027
Enteroliths, *i*, 753, *ii*, 846
Enzymes, pancreatic, *ii*, 1026
  salivary, *i*, 593
Eosinophilia, *i*, 197, 346
  asthma, *i*, 346
  trichinae, *i*, 211, 214
Ependymitis, *iii*, 1851
Epicardium, *i*, 18
Epidermolysis, *iii*, 2089
Epididymis, *ii*, 1475, 1476
  chromaffin cells, *ii*, 1277
  epididymitis, *ii*, 1484, 1487
  tuberculosis, *ii*, **1487**
Epiglottis, *i*, 305, 318
  syphilis, *i*, **317**
  typhoid ulcers, *i*, **314**
Epiphysis of bone, *ii*, 1137, 1155, 1171
  of endosteum, *ii*, **1059**
Epispadia, *ii*, 1424, 1448, 1477
Epistaxis, *i*, 293
Epithelioma, foot, *iii*, **2198**
  epithelioma molluscum, *iii*, **2156**
Epizoa, *iii*, **2155**
Epulis, *i*, **573,** *ii*, 1215
Erosions, aneurysm, *i*, 135, 140, 148, *ii*, 1069, 1087, 1214
  arteries, *i*, 123
  of bone, *ii*, 1087
  of stomach, *i*, 662
  teeth, *i*, 584
Eructations, *i*, 715
Eruption of teeth, *i*, 583
Erythema, *i*, 548
Erythroblasts, *i*, 188
Erythrocytes, *i*, 186
  in bone marrow, *i*, 287
Esophagomalacia, *i*, 632
Esophagus, *i*, 629
  actinomycosis, *i*, 638
  bacteria, *i*, 636
  carcinoma, *i*, **640, 642, 644, 645, 647**
  cardiospasm, *i*, 650
  catarrh, *i*, 634
  congenit. malformations, *i*, 630, **631**
  corrosion, *i*, 638
  cysts, *i*, 638
  diphtheria, *i*, 636
  diverticuli, *i*, 652
  ectasia, *i*, 648, **649**
  esophagism, *i*, 650
  fistulae, *i*, 631, 656
  foreign bodies, *i*, 656
  granulomas, *i*, 637
  hemorrhage, *i*, 634

Esophagus, inflamm. chr., *i*, 634, 635
  lymph nodes, *i*, 646
  oidium albicans, *i*, **561,** 657
  parasites, *i*, 657
  peptic ulcers, *i*, 633
  perforation, *i*, 634, 656, 657
  phlegmonous inflamm., *i*, 637
  poisons, *i*, 638
  post-mortem findings, *i*, 632
  pseudomembranes, *i*, 636
  pulsion diverticuli, *i*, 653, **655**
  pustular inflamm., *i*, 636
  sarcoma, *i*, 639
  stenosis, *i*, 632, 648
  syphilis, *i*, 638
  thrush, *i*, **561**, 657
  traction diverticuli, *i*, **651,** 652
  tuberculosis, *i*, 637
  tumors, *i*, 639
  ulcers, *i*, 633, **642**
  varices, *i*, 633
  veins, *i*, 632
Eunuch, *ii*, 1186
Eustachian tube, *i*, 295
Eustrongylus, *ii*, 1402
Exanthemata, *iii*, 2075
  measles, *iii*, 2076
  scarlet, *iii*, 2076
Exophthalmus, *i*, 516
Exostosis, *ii*, 1083, 1195, **1197,** 1198, **1199,** *iii*, **2053**
Extrauterine gestation, *ii*, 1603, 1609, 1619, *iii*, **1710,** 1737
  ovarian, *ii*, 1619
  tubal, *ii*, 1603
Extrophy of bladder, *ii*, **1423**
Exudate, pleural, *i*, 487
Eye, arcus senilus, *iii*, 2160
  coloboma, *i*, 545
  conjunctivitis gonorrh., *ii*, 1453
  cyclopia, *i*, 547
  degeneration, *iii*, 2015
  elephantiasis of eyelid, *iii*, **2025**
  embolism of retinal artery, *i*, **119**
  gonorrhea, *ii*, 1453
  ophthalmia, *ii*, 1453
  panophthalmia, *iii*, 1809
  retinal glioma, *iii*, 1920
  retinal tumors, *iii*, 1920
  retinitis, *i*, 119

FACE, aprosopia, *i*, 547
  clefts, *i*, 545
  hemiatrophy, *ii*, 1070
  leontine, *ii*, 1112
  nevi, *iii*, **2181, 2182, 2183**
Fallopian tubes, *ii*, 1589
   abscess, *ii*, 1592
   actinomycosis, *ii*, 1600
   appendicitis, *ii*, 1596
   bacteria, *ii*, 1594, 1596
   carcinoma, *ii*, 1598, **1601**
   circulat., *ii*, 1591
   cysts, *ii*, 1554, 1596
   diverticuli, *ii*, 1592
Fallopian tubes, ectop. gest., *ii*, 1590, 1601, 1604, 1606
   gonorrhea, *ii*, 1593, 1596
   hematosalpinx, *ii*, 1591, 1616
   hemorrhages, *ii*, 1591, 1608
   hydatids of Morgagni, *ii*, 1464, 1590
   hydrops, *ii*, 1594, **1595**
   hyperplasia, *ii*, 1592
   inflammation, *ii*, 1594
   kidney (primitive-misplaced), *ii*, 1593, *iii*, 1661, 1662,
   ligaments of Hunter, *ii*, 1612
   lymphangitis-puerperal, *ii*, 1603
   malformation, *ii*, 1590
   Muellers duct, *iii*, 1662
   ovum, *ii*, 1590
   parasites, *ii*, 1601
   perisalpingitis, *ii*, 1595
   peritonitis, *ii*, 1594
   phosphorus-poisoning, *ii*, 1591
   pregnancy, *ii*, 1603, 1604, 1609
   pyosalpinx, *ii*, 1595
   retrohematocele, *ii*, 1608
   rupture, *ii*, 1606, 1608
   sacs, *ii*, 1595
   salpingitis, *ii*, 1592, **1595**
   spermatozoa, *ii*, 1590
   syphilis, *ii*, 1600
   torsion, *ii*, 1591
   tubal pregnancy, *ii*, 1601
   tuberculosis, *ii*, 1594, **1598**
   tuboovar. cysts., *ii*, 1596
Falx cerebri, *i*, **1821**
Fat absorption, *i*, 220
Fat embolism, *i*, 36
  bone marrow, *i*, 288
  glomeruli, *ii*, **1310**
  lung, *i*, 376, 386, 387
Fat infiltration, liver, *ii*, **902**
  pancreas, *ii*, 1034
Fat necrosis, *ii*, 1022, 1038, **1041**
Fat phanerosis, *i*, 40
Fat reaction, *i*, 39
Fat sclerema, *iii*, 1679
Fatty degeneration, arteries, *i*, 101
   glomeruli, *ii*, **1320**
   heart, *i*, 22, 51, 61
   kidney, *ii*, 1301, 1319, **1320**
   liver, *ii*, 902
   lymph glands, *i*, 285
   vessels, *i*, 101
Favus, *iii*, **2149**
Fecal-abscess, *ii*, 876
  calculi, *i*, 753
  fistulas, *i*, 740, *ii*, 842
  impaction, *i*, 753
  stasis, *i*, 749
  vomiting, *i*, 761
Feces, *i*, 743, 751, 758, 777
Feet, *ii*, **1270**
Femur, atrophy, *ii*, **1068, 1142, 1153, 1207**
Fetal adenoma, *i*, **513**
Fetus, abortion, *ii*, 1621, 1632, *iii*, 1737
bacteria, *iii*, 1732
blood mole, *i*, 171, *iii*, 1736

- Fetus, bone, *ii*, 1054
  - cyclops, *i*, **547**
  - death, *iii*, 1735, 2033
  - deformities, *i*, **544,** *ii*, 1169
  - fetal membranes, *iii*, 1710, 1719
  - genito-urinary syst., *ii*, 1424
  - harelip, *i*, **545**
  - infections, *iii*, 1732
  - intrauterine death, *iii*, 1735, 2033
  - intrauterine fractures, *ii*, 1177
  - lithopedion, *ii*, **1610,** 1736
  - lung, *i*, 360
  - micrognathia, *ii*, 1170
  - micromelia, *ii*, **1170,** 1175, **1178**
  - papyraceous, *iii*, 1736
  - syphilis, *iii*, 1718, 1719
  - tuberculosis, *iii*, 1732
  - tumors, *iii*, 1735
  - twins, *iii*, 1724
  - umbilical cord, *iii*, 1733
- Fever, black water fr., *i*, 186
  - puerperal, *iii*, 1754
  - recurrent, *i*, 215, 752
  - scarlet, *iii*, 2076
  - spotted, *i*, 213, 782
  - typhoid, *i*, 213, 761
  - yellow, *i*, 214
- Fibroblasts, *ii*, 1052
- Fibroendothelioma (psamm.), *iii*, **1817, 1818**
- Fibrolipoma kidney, *ii*, **1390**
- Fibroma, bone, *ii*, 1200
  - kidney, *ii*, 1390
  - larynx, *i*, 323
- Fibromyoma uterus, *iii*, **1647**
    - sarcomatous degeneration, *iii*, **1664**
- Fibrosarcoma, *iii*, **2190**
- Filaria nocturna, *i*, **211**
    - filariasis, *i*, 184, 210
- Fingers, clubbed, *ii*, **1115**
  - drumstick, *ii*, 1082
  - Dupuytren's contractions, *ii*, 1244
  - enchondroma, *ii*, **1200**
  - frost-bite, *iii*, **2085**
  - fungoid carcinoma, *iii*, **2212**
  - gout, *ii*, 1254
  - Heberdons's nodes, *ii*, 1254
  - Osler's nodes, *i*, 38
- Fissures, anal, *ii*, 841
  - skull, *ii*, 1084
- Fistula, anal, *i*, 740, *ii*, 842
  - arteriovenous, *i*, 149
  - bladder, *ii*, 1432
  - branchiogenic, *i*, 329
  - esophageal, *i*, 328, 631, 656
  - fecal, *i*, 740, *ii*, 842
  - rectal, *i*, 740, *ii*, 842
  - rectovaginal, *iii*, 1699, 1700, 1708
  - salivary, *i*, 596
  - tracheal, *i*, 328
  - umbilical, *i*, 726
  - urinary, *ii*, 1432
- Flagellates, *ii*, 857
- Flatulence, *i*, 749
- Fleas, *i*, 406, *iii*, 2155
- Flies, chrysops-horsefly, *i*, 262
- Flies, glossina palp-tsetse, *i*, 212
  - myiasis, *i*, 305
- Floating kidney, *ii*, 1298
- Fontanelles, *ii*, 1164
- Foot, abnormal, *ii*, 1270
  - carcinoma, *i*, **169**
  - Chinese of women, *ii*, 1271
  - corns, *iii*, **2166**
  - gummas, *iii*, **2139, 2140**
  - hallux, *ii*, 1270
  - melanosarcoma, *iii*, **2193, 2194**
  - syphilis, *iii*, **2136**
  - talipes, *ii*, 1270
- Foramen ovale, *i*, **92**
    - of Winslow, *i*, 738
- Foreign bodies, in bladder, *ii*, **1447**
    - in blood, *i*, 206
    - in bronchi, *i*, 342, 356
    - in esophagus, *i*, 656
    - in heart, *i*, 86
    - in intestines, *ii*, 834
    - in larynx, *i*, 327
    - in lung, *i*, 406
    - in nose, *i*, 304
    - in peritoneum, *ii*, 870, 882
    - in stomach, *i*, 717
    - in vagina, *iii*, 1691, 1700
- Eoreign body giant cells, *i*, 244
- Fractures, *ii*, 1081, **1089,** 1090
  - green stick, *i*, 183
  - impacted, *ii*, **1090**
  - larynx, *i*, 326
  - spontaneous, *ii*, 1067, **1225**
  - vertebrae, *iii*, 2006
- Fragmentation of myocardium, *i*, 70
- Freezing, *iii*, **2085**
- Friedlander's bacillus, *i*, 295
- Friedreich's disease, *iii*, 2005
- Fungus diseases, actinomycosis, see there,
      - breast, *iii*, 1803
    - oidium, *i*, 549, **561**
    - skin, *iii*, **2118, 2120, 2121, 2149, 2156**
    - sporotrichosis, *i*, 621
    - tongue, *i*, 560, **561**
    - vagina, *iii*, 1698
- Funnel breast, *ii*, 1163
- Furuncle, *iii*, 2105, 2220

- GALACTOCELE, *iii*, 1765, 1802
- Gall bladder, *ii*, 978
  - ampulla of Vater, *ii*, **998**
  - anatomy, *ii*, 978
  - atrophy, *ii*, 1000
  - bacteria, *ii*, 981, 989
  - bile ducts, *ii*, 979
  - bile pigment, *ii*, 987, 1011, 1013
  - bile thrombus, *ii*, 1014
  - calculi, *ii*, 982, 984, 988, 991, **993, 994, 996, 998,** 1000, 1006
  - carcinoma, *ii*, 1002, **1003, 1005**
  - cholangitis, *ii*, 981
  - cholecystitis, *ii*, 984, **1029**
  - cholelithiasis, *ii*, 983
  - common duct, *ii*, **993**
  - empyema, *ii*, 1000

Heavy face type denotes an illustration.

- Gall, gall stones, *ii*, 982
  - hydrocholecystitis, *ii*, 1000
  - icterus, *ii*, 981, 1007, 1012, 1017
  - icterus neonatorum, *ii*, 1017
  - infections, *ii*, 1019
  - inflammation, *ii*, 981
  - jaundice-obstructive, *ii*, 1000
  - Luschka's ducts, *ii*, 979, 997
  - malformation, *ii*, 979
  - occlus. comm. duct, *ii*, 999
  - parasites, *ii*, 1008
  - passage of gall stones, *ii*, 992, 993
  - pericholangitis, *ii*, 982
  - poisons, *ii*, 981, 1012, 1015
  - purulent inflamm., *ii*, 982
  - pyocholecystitis, *ii*, 982
  - sarcoma, *ii*, 1002
  - spirochetae, *ii*, 1020
  - syphilis, *ii*, 1001
  - tuberculosis, *ii*, 1001
  - tumors, *ii*, 1002
  - typhoid, *ii*, 981, 1001
  - ulcers, *ii*, 995
  - Weil's dis., *ii*, 1019
- Gall stones, *ii*, 982, 984, **985, 986, 987,** 988, 991, **993, 994, 996,** 1006
  - passage, *ii*, 992
- Ganglions, ganglion neuroma, *ii*, 1288, *iii*, 1931, **2023**
  - semilunar, *ii*, 1024
- Gangrene, arteries, *i*, **104, 105, 106,** 120, 122
  - decubital, *i*, 337, 485, 627, **628,** *iii*, 2108
  - diabetic, *i*, **104, 106**
  - from freezing, *iii*, **2085**
  - gas gangrene, *iii*, 2042
  - lungs, *i*, 400, 402, 411
  - mouth, *i*, 551
  - Raynaud's symmetrical, *iii*, 2110, 2147
  - senile, *i*, **106**
- Gartner's ducts, *ii*, 1459, 1464
- Gas bacillus—gas edema, *iii*, **2042, 2043, 2044, 2045**
- Gastric ulcers, *i*, 671, 677, 678
- Gastritis, *i*, 666, 713
- Gastromalacia, *i*, 658
- Gastroptosis, *i*, 716
- Gaucher's splenomegaly, *i*, 236
- Genu valgum and varum, *ii*, 1072, **1270,** 1272
- Geographical tongue, *i*, 554
- Gerontoxon, *iii*, 2160
- Giant cell sarcoma, *i*, 573, *ii*, **1191, 1192, 1194, 1214**
- Giant cells, bone marrow, *i*, 286
  - of Dorothy Reed, *i*, 268
  - foreign body, "g. c.," *i*, 244
  - Langerhans, *i*, 10, *iii*, 1712, 1745
  - in lung, *i*, 423
  - in lymphatics, *i*, 180
  - in mouth, *i*, 573
- Giantism, *ii*, 1082, 1150, 1186
- Gingivitis, *i*, 548
- Gland diseases, adenoids, *i*, 301, 618
  - anthracosis, *i*, 174, 250, 254
  - granulomas, *i*, 270
  - Hodgkin's d., *i*, 193
- Gland diseases, Mikulicz's disease, *i*, 604
  - tonsilitis, *i*, 606
- Glanders, *i*, 174
  - in blood, *i*, 213
  - bronchi, *i*, 130, 350
  - larynx, *i*, 320
  - liver, *ii*, 945
  - lung, *i*, 465
  - lymph nodes, *i*, 252
  - lymphatics, *i*, 175
  - mouth, *i*, 559
  - nose, *i*, 298
  - pharynx, *i*, 621
  - spleen, *i*, 243
  - testicles, *ii*, 1494
  - tongue, *i*, 559
- Glands, adenoids, *i*, 301, 618
  - adrenals, *ii*, 1276, 1481
  - Bartholin's, *iii*, 1702, 1707
  - Blandin-Nuhn gl. of tongue, *i*, 575
  - bronchial, *i*, 340
  - Brunner's, *i*, 716
  - carotid, *i*, 330
  - coccygeal, *i*, 331
  - Cowper's, *ii*, 1457
  - hypophysis cerebri, *iii*, 1945
  - lachrymal, *i*, 604
  - Lieberkühn, *i*, 718
  - Littre's, *ii*, 1451, 1453
  - lymph glands, *i*, 248
  - of mouth, *i*, 593
  - parathyroid, *i*, 507
  - parotid, *i*, 593
  - pineal, *iii*, 1945, **1957**
  - pituitary, *iii*, 1945, **1948**
  - puberty, *ii*, 1480
  - salivary, *i*, 182, 593, **598**
  - sebaceous, *iii*, 2216
  - sex gl., *ii*, 1460
  - sublingual, *i*, 507, 575
  - sweat gl., *iii*, 2220
  - thymus, *i*, 495
  - thyroid, *i*, 504
  - of tongue, *i*, 507
  - tonsils, *i*, 606
  - Tyson's, *ii*, 1533
  - Zuckerkandl, *ii*, 1277
- Glioma, *iii*, **1842,** 1921, **1922, 1923, 1924, 1925, 1926, 1927, 1928, 1929, 1930**
  - traumatic, *iii*, 1931
- Glomerular changes, *ii*, 1328, 1343
- Glomerulitis, capillary, *ii*, **1334**
- Glomerulonephritis, *ii*, **1321, 1330, 1333,** 1336, 1340, **1342, 1343,** 1347
  - of scarlet, *ii*, **1329**
- Glomerulus fat embolism, *ii*, **1310**
  - fatty degeneration, *ii*, **1321**
- Glossina palpalis (trypanosomyasis), *i*, 212
- Glossitis, *i*, 548, 559
- Glossocele, *i*, 566
- Glottis, *i*, **307**
- Glycogen in kidney, *ii*, 1324
  - in liver, *ii*, 949
- Glycosuria and adrenalin, *ii*, 1278, *iii*, 1951
- Gnathochisis, *i*, 546

Heavy face type denotes an illustration.

- Goiter, *i*, 501, **518**
  - adenoma, *i*, 512
  - Basedow's disease, *i*, 516, **519**
  - cachexia, *i*, 527
  - calcification, *i*, 521
  - carcinoma, *i*, **530**
  - colloid, *i*, **511**
  - cretinism, *i*, 523
  - cystic g., *i*, **512,** 520
  - etiology, *i*, 502
  - exophthalmus, *i*, 516
  - fetal adenoma, *i*, **514**
  - goiter regions, *i*, 505, 523
  - Grave's disease, *i*, 516
  - hemorrhage, *i*, 521
  - hyperplasia, *i*, 515
  - inflammations, *i*, 510
  - mongolianism, *i*, 526
  - myxedema, *i*, 529
  - ossification, *i*, **521**
  - parathyroids, *i*, 540
  - postbranchial g., *i*, **532**
  - proliferating g., *i*, **531**
  - purpura neonatorum, *i*, 509
  - sarcoma-metast., *i*, **535**
  - substernal g., *i*, 501
  - tetany, *i*, 526
  - thyroiditis, *i*, 508
  - tuberculosis, *i*, 529
  - tumors, *i*, 530
- Gomphosis, *ii*, 1090
- Gonorrhea, anal, *ii*, 845
  - bladder, *ii*, 1452
  - children, *ii*, 1693
  - conjunctivitis, *ii*, 1453
  - endocarditis, *i*, **34,** 35
  - gonococci, *ii*, 1449
  - joints, *ii*, 1237
  - lymphatics, *i*, 173
  - ophthalmia neonat., *ii*, 1453
  - oral, *i*, 516, 548
  - penis, *ii*, 1534
  - prostate, *ii*, 1449
  - rectum, *ii*, 845
  - testes, *ii*, 1484
  - tubes, *ii*, 1593, 1596
  - urethra, *ii*, 1449
  - uterus, *ii*, 1631, *iii*, 1718
  - vagina, *iii*, 1693
  - vulva, *iii*, 1702, 1747
- Gout, *ii*, 1252, 1375
  - tophi, *ii*, **1253**
- Granulomas, bone, *ii*, 1122
  - esophagus, *i*, 637
  - fungoides, *iii*, **2118, 2119, 2120**
  - glands, *i*, 270
  - heart, *i*, 82
  - inguinale, *ii*, **1536**
  - lymph glands, *i*, 270
  - nose, *i*, 297
  - pediculatum, *iii*, **2116**
  - pericardium, *i*, 16
  - pharynx, *i*, 619
  - polypoid, *i*, **337**
  - pulp granuloma, *i*, **578**
- Granulomas, salivary glands, *i*, 595
  - spleen, *i*, 240
  - teeth, *i*, 586
- Granulomatosis lymph glands, *i*, 270
- Grave's disease, *i*, 516
- Greenstick-fracture, *ii*, 1083
- Growth, acromegaly, *ii*, 1082, 1113, 1187
  - giantism, *ii*, 1082, 1150, 1186
  - myxedema, *i*, 529, *ii*, 1181
  - nannasomia, *ii*, 1179
- Gubernaculum, *ii*, 1460, 1476
- Gummas, *iii*, **2047**
  - liver, *ii*, 938, 939, 940, 941, 943
  - lung, *i*, 465
  - mouth, *i*, 556
  - nerves, 2147
  - skin, *iii*, 2138, **2139, 2140**
  - testes, *ii*, 1491, 1492
  - thyroid, *i*, 529
- Gums, *i*, 548, 573
  - carcinoma, *i*, 182, 572
  - endothelioma, *i*, 182
  - epulis, *i*, **573,** *ii*, 1215
  - gingivitis, *i*, 548
  - inflammat., *i*, 57
  - lead line, *i*, 551
  - pyorrhea, *i*, 578
  - scurvy, *i*, 550, *iii*, 2073
  - tumors, *i*, 572
- Gynecomastia, *iii*, 1758, 1759, **1760, 1783**

- Hair, alopecia, *iii*, 2221
  - calvitis, *iii*, 2221
  - favus, *iii*, 2152
  - fungus diseases, *iii*, 2150
  - herpes tonsurans, *iii*, 2150
  - hypertrichosis, *iii*, 2222
  - plica polonica, *iii*, 2090
  - sycosis, *iii*, 2104, 2154
  - syphilis, *iii*, 2156
  - trichorrhexis, *iii*, 2222
- Halisteresis, *ii*, 1055, 1080
- Hanot's cirrhosis liver, *ii*, 929
- Harelip, *i*, **545**
- Haversian canals, *ii*, 1056
- Hay fever, *i*, 293, 344
- Heart, *i*, 1
  - abscess, *i*, 64, 65
  - actinomycosis, *i*, 17
  - Adam-Stoke's, symptom complex, *i*, 21
  - air embolism, *i*, 207
  - amyloid degen., *i*, 55
  - anemia, *i*, 55, **64**
  - aneurysms, *i*, 32, 43, 58, **69, 70, 146**
  - aorta, *i*, 32, 45, 73, 93, 94, **108, 111, 124, 125, 126**
  - arteries, *i*, **99, 104, 106**
  - Aschoff's nodules, *i*, 64
  - atrophy, *i*, 49, **50,** 73
  - auricles, *i*, 21, 78, 87
  - Buhl's disease, *i*, 53
  - bundle of His, *i*, 9, 20, 21, 22
  - calcification, *i*, 23, 41, 54
  - carcinoma, *i*, **18**
  - cardiac death, *i*, 62

Heart, cardiac, hypertrophy, *i*, 72, 74, 77
  cardiorenal, *i*, 42, *ii*, 1314, 1349, 1353
  changes in size, *i*, 71, 72
  coagula, *i*, 72, 81
  coagulation necrosis, *i*, 58
  congenital heart lesions, *i*, 28, 47, 86, 89
  conus pulmonalis, *i*, 92, 97
  cor villosum, *i*, 7
  coronary arteries and veins, *i*, 55, 56, **57**
  cyanosis, *i*, 44, 53, 55, 56
  death sudden, *i*, 62
  defects, *i*, 86, 89
  degenerations, *i*, 22, **50**
  diabetic gangrene, *i*, 104
  diastole, *i*, 46
  dilatation, *i*, **44, 45,** 74, 77
  diphtheria, *i*, 61, 65
  diverticuli, *i*, 96
  ductus arteriosus, *i*, 95, **97**
  embryology, *i*, **87**
  endocardium, *i*, 19, 25
  epicardium, *i*, 1, 4, **18,** 22, 51, 61
  epistaxis, *i*, 293
  fat infiltration, *i*, **50**
  fatty degeneration, *i*, **50, 51**
  fatty heart, *i*, 5, 19, 54
  fibrosis, *i*, **67**
  foramen ovale, *i*, **92**
  foreign bodies, *i*, 86
  fragmentation, *i*, 70
  gas edema, *iii*, **2042**
  granulomas, *i*, 82
  hanging, death by, *i*, 71
  heart block, *i*, 20, 21
  heart failure, *i*, 41, 42, *ii*, 1623
  hemorrhage, *i*, 3, 5, 16, 21
  hydropericardium, *i*, 2, 145
  hypertrophy, *i*, 72, 74, 77
  hypoplasia, *i*, 71
  infarcts, *i*, **59**
  ischemia, *i*, 21, 58
  malformation, *i*, 86, 89, 90
  measurements, *i*, 71
  mitral lesions, *i*, 43, **44, 45**
  myocarditis, *i*, 6, 58, 60, **62,** 63, 65, 66
  myocardium, *i*, 48, 86
  nephritis, *i*, 2, 38, 55
  nerves, *i*, 20
  noduli albini, *i*, 29,
  Osler's nodes, *i*, 38
  papillary muscles, *i*, **51,** 66, **67**
  parasites, *i*, 86
  parenchymatous diseases, *i*, 49, 51, 68
  perforation, *i*, **58**
  pericarditis, *i*, **6**
  pericardium, *i*, 1
  plethora, *i*, 77
  poisons, *i*, 5, 52
  postmortem coagula, *i*, 2, 38, 72, 81
  pulsus paradoxus, *i*, 3
  rhabdomyomas, *i*, **84,** *iii*, 2055
  rheumatism, *i*, 28, 63
  rupture, *i*, 4, 54, 69
  sarcoma, *i*, 18, 60, 67, 85, *iii*, **1665**
  scars, *i*, 60, **64, 67,** 68

Heart, segmentation, *i*, 70
  septum defects, *i*, 95
  stenosis, *i*, 91
  syphilis, *i*, 17, 56, 82, **124**
  thrombi, *i*, 26, 56, 78, **79, 80,** 81, **102, 104, 105**
  tricuspids, *i*, 93
  tuberculosis, *i*, 17, 82
  tumors, *i*, 17, **18,** 83
  valvular atheroma, *i*, 22
  valvular insufficiency, *i*, 44
  valvular stenosis, *i*, 42, 93
  vegetations, *i*, 123
  vessels, *i*, **99**
  Winkel's disease, *i*, 53
  wounds, *i*, 4, 5
Heberden's nodules, *ii*, 1254
Helminthiasis, *i*, 760, *ii*, 833
  ankylostoma, *ii*, 853
  ascaris, *ii*, 853
  eosinophilia, *i*, 197
  oxyuris, *ii*, 833, 854
  tenia, *ii*, 847, **849**
  trichinae, *i*, 211, *iii*, 2040, **2056, 2057**
Hemangioma, *i*, 120
  cavernous, *iii*, **2183**
  kidney, *ii*, 1391
Hemangiosarcoma bone, *ii*, **1211, 1212**
Hematidrosis, *iii*, 2071
Hematocele, *ii*, 1513
Hematocolpos, *ii*, 1616
Hematoma, abd. rectus muscle, *iii*, **2034**
  cephalic, *ii*, **1093**
  in Moeller Barlow's disease, *ii*, 1167, **1168**
  ovary, *ii*, 1548
  vagina, *iii*, 1699
  vulva, *iii*, 1701
Hematometra, *ii*, 1616
Hematoporphyria, *ii*, 1231
Hematosalpinx, *ii*, 1591, 1616
Hematuria, renal, *ii*, 1309, 1333, 1528
Hemiatrophy face, *ii*, 1070
Hemicephalia, *iii*, **1856, 1857**
Hemiplegia, *iii*, 1869
Hemoconia, *i*, 188
Hemoglobin, *i*, 189
  of spleen, *i*, 219
Hemoglobinemia, *i*, 186
Hemoglobinuria, *i*, 186
Hemolymph nodes, *i*, 250
Hemolysin, *i*, 190
Hemopericardium, *i*, 3, 16
Hemoperitoneum, *ii*, 860
Hemophilia, *i*, 186
Hemopoietic apparatus, *i*, 216, 250, 286
  diseases, anemia, *i*, 191
    bone marrow, *i*, 195, 196, 286
    liver, *i*, 195
    lymph nodes, *i*, 196, 250
    spleen, *i*, 195, 196, 216, 219
Hemoptysis, *i*, 450
Hemorrhages, *i*, 204
  adrenal, *ii*, **1282**
  capillaries, *i*, 171

Hemorrhages, cerebral, *iii*, 1884, **1885**
  esophageal, *i*, 634
  gastric, *i*, 661, 664, 686
  heart, *i*, 3, 16, 21
  intestines, *i*, 757, 793
  kidney, *ii*, 1307, 1361
  larynx, *i*, 307
  liver, *ii*, 899
  lung, *i*, 371, 373, 377
  newborn, *iii*, 1961
  nose, *i*, 299
  pancreas, *ii*, 1022, **1023**
  pericardium, *i*, 3, 16
  peritoneum, *ii*, 860
  pleura, *i*, 483
  spinal, *iii*, 1961
  spleen, *i*, 227, 229
  stomach, *i*, 661, 664, 686.
  testes, *ii*, 1483
  uterus, *ii*, 1617, 1622, 1623
  vagina, *iii*, 1699
  vulva, *iii*, 1701
Hemorrhoids, *i*, 165, **166,** 754, *ii*, 841
Hemosporidia, *i*, 208
Hemothorax, *i*, 483
Hepatic vein, *ii*, 893
Hepatisation of lung, *i*, 392
Hepatitis, *ii*, 909, 921
Hermaphrotism, *ii*, 1466, **1481, 1483**
  pseudohermaphrodism, *ii*, 1291, **1481**
Hernia, abdominal, *i*, 728
  cerebral, *iii*, **1855**
  crural, *i*, 730
  diaphragmatic, *i*, 359, 737
  epigastric, *i*, 738
  femoral, *i*, 734
  foramen of Winslow, *i*, 738
  incarcerated, *i*, 739
  inguinal, *i*, 730, **732, 739**
  internal, *i*, 728, 736
  ischial, *i*, 734
  Littre's, *i*, 734
  lung, *i*, 370
  obdurator, *i*, 734
  pelvis, *i*, **730, 731, 733**
  pericecal, *i*, 737
  perineal, *i*, 734
  retroperitoneal, *i*, 737
  sigmoidal, *i*, 738
  strangulated, *i*, **739**
  umbilical, *i*, **735**
  ventral, *i*, 736
Herpes, *iii*, 2086
  facial, *iii*, 2086
  herpes zoster, *iii*, 2086
  prepuce, *iii*, 2086
Hipjoint, ankylosis, *ii*, **1263**
  caries, *ii*, **1256**
  congenit. luxation, *ii*, 1269
  tuberculosis, *ii*, **1256**
Hirschsprung's disease, *i*, 720, **721,** 736
Hodgkin's disease, *i*, 193, 266, 271
Homosexuals, *ii*, 1482
Hookworms, *ii*, 853
Horseshoe-kidney, *ii*, **1295**
Hourglass stomach, *i*, 660, 687
Howell-Jolly bodies, *i*, 188
Hutchinson teeth, *i*, 584
Hyalin degeneration, arteries, *i*, 106
    heart, *i*, 23
    joints, *ii*, 1243
    kidney, *ii*, 1322, **1323**
    lymph glands, *i*, 285
    pancreas, *ii*, 1033
    thyroid, *i*, 521
    vessels, *i*, 106
Hydatid cysts of Morgagni, *ii*, 1464, 1590
Hydatidiform mole, *iii*, 1698, **1722, 1723, 1724**
Hydradinoma, vulva, *iii*, **2200**
Hydramnion, *iii*, 1720
Hydremia, *i*, 185
Hydrocele, *ii*, 1484, 1511, **1512**
Hydrocephalus, *ii*, 1164, **1166,** *iii*, 1823, 1832
Hydrochloric acid, *i*, 657, 679, 708
Hydrocholecystitis, *ii*, 1000
Hydroencephalocele, *iii*, **1854**
Hydrometra, *ii*, 1616
Hydronephrosis, *ii*, 1297, 1299, 1403, **1404 1406, 1408, 1414,** 1528
Hydropericardium, *i*, 2, 145
Hydrophobia, *iii*, 1901
  Negri bodies, *iii*, 1900
Hydropic degen. of muscle, *iii*, **2037**
Hydrops, ascites, *i*, 176
  gall bladder, *ii*, 1000
  kidney, *ii*, **1323**
  pericardium, *i*, 2
  peritoneal, *ii*, 860
Hydrorrhea, *iii*, 1714
Hydrosalpinx, *ii*, **1595**
Hydrothorax, *i*, 375, 482
Hygroma, cystic of neck, *i*, **177,** 178. *iii*, **2066**
  dura, *iii*, **1814**
  prepatellar, *iii*, **2065**
  of tendon-sheaths, *iii*, 2063, 2066
Hymen, *iii*, 1700
Hyperinosis, *i*, 186
Hyperkeratosis tongue, *i*, 565
Hypernephroma, *ii*, 1225, 1287 1290, 1385, **1395, 1396, 1397, 1398, 1399, 1400**
  bone, *i*, 167, *ii*, 1229, 1290
  metastasis to adrenals, *ii*, 1225, 1287, 1290
Hyperostosis, *ii*, 1083, 1107, 1113
Hyperplasia, *i*, 167
  lymphatics, *i*, 176
  spleen, *i*, 231, 234, 239
  thyroid, *i*, 509, 515
Hypertrophy, adrenal, *ii*, 1280
  aorta, *i*, 151
  arteries, *i*, 151
  bladder trabeculae, *ii*, **1443, 1523**
  heart, *i*, 72, 74, 77
  joints, *ii*, 1232
  lungs, *i*, 373
  prostate, *ii*, **1521, 1522, 1523, 1524**
  thyroid, *i*, 509
Hypoinosis, *i*, 186
Hypophysis, *ii*, 1180, *iii*, 1945
Hypospadia, *ii*, **1477**

Heavy face type denotes an illustration.

ICHTHYOSIS, *iii*, 2171
Icterus, *i*, 222, *ii*, 981, 1009, 1012
  familial hemolytic, *i*, 192
  infections, *i*, 214, 610, *ii*, 1019
  kidney, *ii*, 1301
  neonatorum, *ii*, 1017, *iii*, 2038
  obstructive, *ii*, 1000
  Weil's disease, *ii*, 1019
Ileum, *i*, 718
  carcinoma, *ii*, **818, 823**
  diphth. inflamm., *i*, **769**
  obduration, *i*, **784**
  sarcoma, *ii*, **825**
Ileus, *i*, 744, 747, 752, 757
Impaction, *i*, 753
Impetigo, *iii*, 2091
Incarceration, *i*, 739, 748
Infarcts, anemic infarcts, *i*, 227, *ii*, **1303, 1306, 1307**
  argyria, *ii*, **1381**
  calcium infarct, *iii*, 1878
  fat infarct, *ii*, 1381
  heart, *i*, 59
  intestines, *i*, 754, 756
  kidney, *ii*, **1303, 1304, 1305, 1306, 1307, 1308,** 1375, 1381, 1382
  lung, *i*, 379, 384
  placenta, *iii*, **1728**
  silver infarct, *ii*, **1381**
  spleen, *i*, **227,** 228
  uric acid infarct, *ii*, 1375
Infections, aneurysm, *i*, 147
  arteries, *i*, 115, 214
  bacterial, *i*, 213
  blood, *i*, 213, 262, 305, 781
  bone, *ii*, 1096
  bone marrow, *i*, 290
  gall bladder, *ii*, 981, 999
  heart, *i*, 15
  intestines, *i*, 761, 770
  joints, *ii*, 1235, 1237, 1255
  larynx, *i*, 309, 311, 312, 315, 316, 318, 319
  liver, *ii*, 911, 913, 932, 937
  lungs, *i*, 386, 389, 405, 406, 419, 422, 461, 465, 466
  lymph nodes, *i*, 250, 252, 255, 258, 262
  lymph vessels, *i*, 173
  mouth, *i*, 549, 559
  nose, *i*, 293, 301
  pancreas, *ii*, 1032, 1033
  parasitic, *i*, 208
  parotid, *i*, 595
  peritoneum, *ii*, 867, 872
  pharynx, *i*, 608, 619, 621
  puerperal, *i*, 171, *iii*, 1702
  salivary glands, *i*, 595
  skull, *i*, 159
  spirillae, *i*, 214
  spirochetae, *i*, 214, 215
  spleen, *i*, 225, 235, 243
  stomach, *i*, 661, 670, 672
  teeth, *i*, 578
  tongue, *i*, 317, 556, 559
  veins, *i*, 160
  vertebrae, *ii*, 1130
Infections, vessels, *i*, 115
  Weil's disease, *i*, 214, 219
Influenza, *i*, 296, 312, 341, 389, 403
  bronchi, *i*, 341
  influenza bacilli, *i*, 341
  larynx, *i*, 312
  lung, *i*, 389, 403
  Pfeiffer's bacilli, *i*, 341
  thyroid, *i*, 312, 341, 389, 403
Infusoria, *ii*, 858
Insufficiency diseases, beri-beri, *iii*, 2016
    pellagra, *iii*, 2002
    rachitis, *ii*, 1151
    scurvy, *i*, 550, *iii*, 2073
    scurvy-infantile-Moeller Barlow's disease, *ii*, 1166, *iii*, 2073
Intertrigo, *iii*, 2090
Intestines, *i*, 717, **830**
  abscesses, *i*, 764, *ii*, 830, 838
  actinomycosis, *i*, 803
  adenofibroma, *i*, **809**
  adhesions, *i*, 744
  amebae, *i*, 772, *ii*, **849,** 857
  amyloid degen., *i*, 758, 805
  anemia, *ii*, 851, 853
  aneurysms, *i*, 757
  ankylostoma, *ii*, **849, 853**
  anthrax, *i*, 803
  anus, *i*, 722, **724,** *ii*, 844, 847
  anus artificial, *i*, 740
  appendicitis, *i*, 718, 747, 776, 803, **816,** *ii*, **817,** 832, **833, 837, 839**
  arsenic-poisoning, *i*, 781
  arteries and veins, *i*, 749, 753, 755, 756, *ii*, 845
  ascaris, *ii*, **849,** 853
  atresia, *i*, 723, **724,** 747
  atrophy, *i*, 804
  Auerbach's plexus, *i*, 719
  bacteria, *i*, 751, 760, 773, 783, 785, *ii*, 858
  Bilharzia, *ii*, 856
  blood, *i*, 758
  bothriocephalus, *ii*, **849,** 850
  Brunner's glands, *i*, 716
  carcinoma, *i*, **696, 697,** 811, **810, 814, 815, 816,** *ii*, **817, 818, 819, 820, 821, 823**
  catarrh, *i*, 716
  cecum, *i*, 720, *ii*, 831
  cercomona, *ii*, **849**
  cholera, *i*, 777
  chyme, *i*, 751
  circulation, *i*, 719
  cloaca, *i*, 722
  colitis, *i*, **766,** *ii*, 831
  colon, *i*, 718, 746, 749, *ii*, 831
  concretions, *i*, 753
  congenit. stenosis, *i*, 720
  constipations, *i*, 751, *ii*, 845
  constrictions, *i*, 727
  coproliths, *i*, 753, *ii*, 846
  coprostasis, *i*, 751
  cords, *i*, 726
  crural hernia, *i*, 730
  cysticercus, *ii*, 848
  cysts, *i*, 727, 764

- Intestines, decubitus, *ii*, 845
  - degenerations, *i*, 604
  - diaphragmatic hernia, *i*, 737
  - diarrhea, *i*, 761, 763
  - dilatation, *i*, 749, **752**
  - diphtherit. inflamm., *i*, 768, 744, **769**
  - distension, *i*, 750
  - distomum, *ii*, **849**, 856
  - diverticuli, *i*, 725, **740**, **749**
  - Douglas's cul de sac, *ii*, 883
  - duodenum, *i*, 718, *ii*, 829
  - dysentery, *i*, **765**, **768**, 770, 772, 773, 775, **776**
  - edema, *i*, 755
  - embolism, *i*, 735, 756
  - embryology, *i*, 722
  - emphysema, *i*, 765
  - enema-ulcers, *ii*, 845
  - enteritis, *i*, 758, 763, 767, 771
  - enteroliths, *i*, 753, *ii*, 846
  - enteroptosis, *i*, 716
  - epigastric hernia, *i*, 738
  - fat polyps, *i*, **775**
  - fecal impaction, *i*, 753
  - fecal stasis, *i*, 749
  - fecal vomiting, *i*, 761
  - fecoliths, *i*, 753, *ii*, 846
  - femoral hernia, *i*, 734
  - fissures, *ii*, 841
  - fistulas, *i*, 740, *ii*, 842
  - flatulence, *i*, 749
  - foramen of Winslow, *i*, 738
  - foreign bodies, *ii*, 834
  - gonorrhea, *ii*, 845
  - hamartomas, *ii*, 819
  - hemorrhage, *i*, 757, 793
  - hemorrhoids, *i*, 754, *ii*, 841
  - hernias, *i*, 728, 736
  - Hirschsprung's disease, *i*, 720, **721**, 736
  - hookworm, *ii*, 853
  - hyperemia, *i*, 753
  - ileum, *i*, **697**, 718, **742**, **748**, **769**, *ii*, **818**, **823**, **825**
  - ileus, *i*, 744, 747, *ii*, 852, 882
  - impaction, *i*, 753
  - incarceration, *i*, 739, 748
  - infarction, *i*, 754, 756
  - infection, *i*, 761, 770
  - inguinal hernia, *i*, 730
  - internal hernia, *i*, 728, 736
  - intussusception, *i*, **741**, **742**, 745
  - ischemia, *i*, 740
  - ischiatic hernia, *i*, 734
  - jejunum, *i*, 718
  - kinking, *i*, 747
  - leprosy, *ii*, 846
  - leucemia, *i*, 805
  - Lieberkuhn's glands, *i*, 718
  - lipoma, *i*, **708**, **807**
  - Littre's hernia, *i*, 734
  - louse, *i*, 782
  - lymphatics, *i*, 718
  - malformation, *i*, 719
  - measurements, *i*, 719
  - Meckel's diverticulum, *i*, 725, 748
  - meconium, *i*, 719, *ii*, 859
- Intestines, Meissner's plexus, *i*, 719
  - melanosis, *i*, 759, 804
  - membranous enteritis, *i*, 767
  - mercury poisoning, *i*, 770
  - myomas, *i*, 806
  - obturation, *i*, **747**
  - obturator-hernia, *i*, 734, 748
  - omentum, *i*, 747
  - oxyuris, *ii*, 833, **849**, 854
  - pancreatic tissue, *i*, 728
  - paralysis, *i*, 744, 751
  - parasites, *i*, 760, *ii*, **833**, 847, **849**, **853**, 856, **880**
  - paratyphoid, *i*, 761
  - perforation, *i*, 753, 801, *ii*, 837
  - pericecal hernia, *i*, 737
  - perineal hernia, *i*, 734
  - periproctitis, *ii*, 842
  - peritonitis, *i*, 751, 753, 759
  - perityphlitis, *i*, 746
  - Peyer's patches, *i*, 718, 774, 788, 797
  - pigmentation, *i*, 759, 804
  - pneumotosis, *i*, 767
  - poisons, *i*, 761, 770
  - polypi, *i*, 746, 760, 775, **810**, **811**, **812**
  - position changes congenit., *i*, 728
  - post mortem findings, *i*, 736, 780, 782
  - proctitis, *ii*, 842
  - prolapsus, *i*, 741, **743**, 744
  - protozoa, *ii*, 857
  - Prowazeki-bodies, *i*, 782
  - pseudomembrane, *i*, 768
  - ptomains, *i*, 762, 770
  - rectum, *i*, 722, 724, 744, 745, 813, *ii*, **826**, **827**, 841, 845
  - relapsing fever, *i*, 783
  - retroperitoneal hernia, *i*, 737
  - Rickettsia, *i*, 782
  - rose spots, *i*, 781
  - sarcoma, *ii*, 824, **825**, **826**, **827**
  - scars, *i*, 747, 800
  - sigmoid, *i*, 718, 738, 746
  - sigmoiditis, *i*, **696**, **721**
  - size, *i*, 719
  - spotted fever, *i*, 781
  - stasis, *i*, 754, 777
  - stenosis, *i*, 747
  - stomach, *i*, 657
  - stools, *i*, 743, 751, 758, 777
  - subphrenic abscess, *ii*, 830
  - syphilis, *i*, 802, *ii*, 842
  - teniae, *ii*, 847, **849**
  - thrombi, *i*, 785
  - torsion, *i*, 722
  - trauma, *i*, 737, *ii*, 845
  - trichinae, *i*, 211, 212, *iii*, 2040, **2056**, **2057**
  - trichocephalus, *ii*, **849**
  - trichomona, *ii*, **849**
  - tuberculosis, *i*, 796, **799**, **800**
  - tularemia, *i*, 262
  - typhlitis, *ii*, 831
  - typhoid, *i*, 761, 783, 787, **788**, **789**, **790**, **791**, **792**
  - typhoid carriers, *i*, 783
  - typhoid relapse, *i*, **792**

- Intestines, typhus, *i*, 781
  - ulcerations, *i*, 757, 765, 774, 788, 798, *ii*, 829, 841, **790, 791**
  - umbilical hernia, *i*, 726, 735
  - veins, *i*, 749
  - ventral hernia, *i*, 736
  - volvulus, *i*, 746
  - vomiting, *i*, 761
  - war typhus, *i*, 782
  - Widal reaction, *i*, 785
- Intubation, *i*, 308
- Intussusception, *i*, 741, 745
- Iodothyreoglobulin, *i*, 528
- Iron metabolism, *i*, 219
- Ischemia, heart, *i*, 21, 58
  - intestines, *i*, 740
  - kidney, *ii*, 1302
- Islands of Langerhans, *ii*, 1035
- Itch, *iii*, 2155
- Ixodes, *iii*, 2155

- JAUNDICE, *ii*, 1009, 1019
- Jejunum, *i*, 718
  - carcinoma, *ii*, **823**
- Joints, *ii*, 1228
  - abscess, *ii*, 1235
  - adhesions, *ii*, 1234, 1244, 1249
  - ankylosis, *ii*, 1234, 1244, **1263**
  - arthritis deformans, *ii*, 1238, **1240,** 1242, **1245,** 1247, **1248**
  - arthritites, *ii*, 1235, **1240**
  - atrophy, *ii*, 1242
  - bursae, *ii*, 1235
  - calcium, *ii*, 1231
  - capsules, *ii*, 1231, 1243
  - caries, *ii*, 1231, **1256**
  - cartilage, *ii*, 1229, 1232, 1256
  - cavities, *ii*, 1229
  - Charcot's joint, *ii*, **1251**
  - chondromatosis, *ii*, 1275
  - circulatory disturbances, *ii*, 1233
  - coxa vara, *ii*, 1072
  - coxitis, *ii*, 1236, 1268
  - degenerations, *ii*, 1243
  - diarthroses, *ii*, 1228
  - dislocations, *ii*, 1086, 1090
  - elbow joint, *ii*, **1274**
  - empyema, *ii*, 1235
  - false joints, *ii*, 1086, 1089
  - feet, *ii*, **1270**
  - genu valgum and varum, *ii*, 1072, 1244, **1270**
  - gonorrhea, *ii*, 1238
  - gout, *ii*, 1252, **1253**
  - hallux, *ii*, **1270**
  - hand, *ii*, 1205, **1248**
  - healing, *ii*, 1240, 1261
  - Heberden's nodes, *ii*, 1254
  - hemorrhage, *i*, 165, *ii*, 1233, 1242
  - hip joint, *ii*, **1256, 1260, 1263,** 1269
  - hypertrophy, *ii*, 1232
  - infection, *ii*, 1235, 1237
  - inflammation, *ii*, 1231, 1234
  - joint mice, *ii*, 1243, 1273, **1274**
  - joints, false, *ii*, 1086, 1089

- Joints, knee joint, *ii*, 1244, 1251, 1259, 1263, 1272
  - kyphoscoliosis, *ii*, 1266
  - kyphosis, *ii*, 1264, **1266**
  - lordosis, *ii*, 1079, 1264
  - luxation, *ii*, 1247
  - luxation, congenital, *ii*, 1269
  - neuropathic arthropathics, *ii*, 1250
  - ochronosis, *ii*, 1230
  - osteoarthritis, *ii*, 1239
  - pelvis (Otto Chrobach's), *ii*, 1266
  - pes equinus-calcaneus, *ii*, **1270**
  - pes planus, *ii*, 1271
  - positions, abnormal, *ii*, **1270**
  - Pott's kyphosis, *ii*, 1130, 1267
  - regression, *ii*, 1232
  - rheumatism, *ii*, 1236
  - rice bodies, *ii*, 1257, 1275
  - scoliosis, *ii*, 1066, 1079, 1264
  - senile changes, *ii*, 1229, 1247
  - spondylitis, *ii*, **1245**, 1268
  - spondylolithesis, *ii*, 1263, 1268
  - suppuration, *ii*, 1237
  - synarthroses, *ii*, 1228
  - synovial fluid, *ii*, 1234
  - synovial membrane, *ii*, 1228, 1243, 1256
  - synovitis, *ii*, 1234
  - syphilis, *ii*, 1261
  - tophi, *ii*, 1253
  - trauma, *ii*, 1233, **1240,** 1242, 1267
  - tuberculosis, *ii*, 1255, **1256**
  - tumors, *ii*, 1262
  - uric acid, *ii*, 1231

- KALA-AZAR, *i*, 212, 236
- Keloid, *iii*, **2174, 2175**
- Keratoma, *iii*, 2172
- Kidney, *ii*, 1292, 1297
  - abscesses, *ii*, 1361, 1364
  - actinomycosis, *ii*, 1374
  - adenoma, *ii*, 1387, **1388**
  - adeno-sarcoma, *ii*, **1392, 1394**
  - albuminous degeneration, *ii*, 1318, 1329
  - albuminuria, *ii*, 1302, 1325
  - amyloid degen., *ii*, 1358, **1359**
  - amyloidosis, *ii*, 1373
  - anatomy, *ii*, 1297
  - anemia, *ii*, 1302
  - anomalies, *ii*, 1293
  - aplasia, *ii*, 1292
  - apoplexy into renal bed, *ii*, 1402
  - argyria, *ii*, **1381**
  - arteriosclerosis, *i*, 107, 115, *ii*, **1312, 1314, 1315, 1331,** 1356
  - artery renal, *ii*, 1303
  - atrophy, *ii*, 1310, **1311,** 1314, 1331, **1406**
  - autointoxication, *ii*, 1316
  - bacteria, *ii*, 1316, 1339, 1361, 1362, 1417
  - bilirubin, *ii*, 1376, 1377
  - bladder, *ii*, 1296
  - blood-pigment, *ii*, 1301, 1309, 1377
  - Bright's disease, *ii*, 1316
  - calcification, *ii*, 1308, 1331, 1378
  - calcium-infarcts, *ii*, 1378

Kidney

- Kidney, calculi, *ii*, 1377, 1381, 1389, **1409, 1411, 1412**
  - capsule, *ii*, 1311
  - carcinoma, *ii*, 1389, 1391, 1419
  - cardio-renal, *ii*, 1314, 1349, 1353, **1408**
  - casts, *ii*, **1326**, 1327
  - cholera, *ii*, 1302, 1316
  - circulatory disturb., *ii*, 1293, 1299, 1302
  - cirrhosis, *ii*, 1314
  - cloudy swelling, *ii*, 1318
  - coagul. necrosis, *ii*, 1302, 1304
  - colic-renal, *ii*, 1416
  - concretions, *ii*, 1377
  - congenital cysts and tumors, *ii*, 1311, 1318, 1382, **1383, 1386**
  - congestion, *ii*, 1299
  - contracted kidney, *ii*, 1312, 1330, **1331**, 1332, 1340, 1348, 1350, **1353**, 1354, **1355**
  - crescents, *ii*, 1335
  - cyanotic induration, *ii*, 1300
  - cystic kidney, *ii*, 1318, 1382, **1383, 1384, 1386**
  - cysticercus, *ii*, 1402
  - cystin, *ii*, 1412
  - cystitis, *ii*, 1363
  - decapsulation, *ii*, 1348
  - defects, *ii*, **1293**
  - degenerations, *ii*, 1315, 1317, 1319, 1322, 1323, 1324, 1358
  - diabetes, *ii*, 1322, 1324
  - diphtheria, *ii*, 1316, **1329**, 1338, 1364
  - displacements, *ii*, 1295, 1298
  - distomum, *ii*, 1402
  - dystopia, *ii*, 1295
  - dystrophy, *ii*, **1295**, 1318
  - echinococcus, *ii*, 1402
  - eclampsia, *ii*, 1302, 1310
  - edema of scrotum, *ii*, 1533
  - embolism, *ii*, 1303, 1306, 1310, **1336**
  - embryology, *ii*, 1292
  - epithelial changes, *ii*, 1318, 1328
  - eustrongylus, *ii*, 1402
  - fat emboli, *ii*. **1310**
  - fat infarcts, *ii*, 1381, 1382
  - fatty degeneration, *ii*, 1301, 1319, **1320, 1321**
  - fibrolipoma, *ii*, **1390**
  - fibroma, *ii*, 1390
  - filaria, *ii*, 1402
  - floating kidney, *ii*, 1298
  - focal nephritis, *ii*, 1332, 1337
  - fusion, *ii*, 1294
  - gas edema, *iii*, **2044**
  - glomerular changes, *ii*, 1328, 1343
  - glomerulitis, *ii*, **1334**
  - glomerulonephritis, *ii*, **1321, 1330, 1333**, 1336, 1337, 1340, **1342, 1343**, 1347
  - glycogen, *ii*, 1324
  - gout, *ii*, 1375
  - granular atrophy, *ii*, 1315
  - Grawitz tumors, *ii*, 1389
  - hamartoma, *ii*, 1390
  - heart failure, *i*, 42
  - hemangioma, *ii*, 1391
  - hematuria, *ii*, 1309, 1333, 1528

Kidney

- Kidney, hemorrhages, *ii*, 1307, 1361, 1402
  - horse shoe kidney, *ii*, **1295**
  - hyalin degenerat., *ii*, 1322, **1323**
  - hydronephrosis, *ii*, 1297, 1299, **1403, 1404, 1405, 1408**, 1414, 1528
  - hydropic degenerat., *ii*, **1323**
  - hyperemia, *ii*, 1299, 1307
  - hypernephroma, *ii*, 1225, 1287, 1290, **1395, 1396, 1397, 1398, 1399, 1400**
  - hypertony, *ii*, 1350, 1353
  - icterus, *ii*, 1301
  - infarcts, *ii*, **1303, 1304, 1305, 1306, 1307, 1308, 1375**
  - inflammation, *ii*, 1315, 1317, 1327
  - interstitial nephritis, *ii*, 1331
  - ischemia, *ii*, 1302
  - juvenile albuminuria, *ii*, 1325
  - large red kidney, *ii*, 1346
  - lead poisoning, *ii*, 1315
  - leucemia, *ii*, 1336, **1374**
  - lipomas, *ii*, 1391
  - malformations, *ii*, 1296, 1403, 1424
  - malignant tumors, *ii*, 1400
  - mercury poisoning, *ii*, 1302, 1316, **1379**
  - metaplasia, *ii*, 1419
  - motility, *ii*, 1295
  - myxomas, *ii*, 1391, 1393
  - necrosis, *ii*, 1302, 1305, 1306, 1310, **1324**
  - nephrectomy, *ii*, 1416
  - nephritis, *ii*, 1320, 1329, 1332, 1338
  - nephritis acute, *ii*, **1329**
  - nephroliths, *ii*, 1377
  - nephropexy, *ii*, 1299
  - nephroptosis, *ii*, 1298
  - nephrosis, *ii*, 1317
  - nephrotomy, *ii*, 1426
  - oxalic acid poisoning, *ii*, 1315, 1381
  - paranephritis, *ii*, 1420
  - parasites, *ii*, 1402
  - parenchym. changes, *ii*, 1335
  - pelvis-renal, *ii*, 1311, 1375, **1403, 1406**, 1407, 1416, 1417
  - perinephritis, *ii*, 1419, 1420
  - phosphorus poisoning, *ii*, 1316, 1322
  - pneumonia, *ii*, 1316, 1338
  - poisons, *ii*, 1315, 1316, 1322, 1379, 1381
  - polycystic (congen.), *ii*, **1386**
  - positions, *ii*, 1295, 1298
  - post mortem changes, *ii*, 1298, 1352
  - pregnancy, *ii*, 1302, 1310, *iii*, 1727
  - primitive kidney, *ii*, 1392, **1458, 1463**, 1593, *iii*, 1661, 1662
  - protagon, *ii*, 1319
  - ptosis, *ii*, 1295
  - pyelitis, *ii*, 1417, 1429
  - pyelonephritis, *ii*, 1362, **1363**, 1528
  - pyelotomy, *ii*, 1416
  - red kidney, ii, **1351**
  - renal bed, *ii*, 1402, 1405
  - renal pelvis, *ii*, 1403, 1406
  - renal vein, *i*, 165
  - rhabdomyoma, *ii*, **1394**
  - sarcoma, *ii*, **1392**, 1419
  - scarlet fever, *ii*, **1329**, 1338, 1339, 1340, 1374

Heavy face type denotes an illustration.

- Kidney, scars, *ii*, 1308
  - senile atrophy, *ii*, 1310
  - sublimate poisoning, *ii*, 1302
  - supernumerary kidneys, *ii*, 1296
  - syphilis, *ii*, 1373, **1384**
  - thrombosis, *ii*, 1300, 1305
  - tophi, *ii*, 1376
  - toxins, *ii*, 1303
  - trauma, *ii*, 1299, 1402
  - tuberculosis, *ii*, 1305, 1322, 1365, **1366, 1369, 1371**
  - tubules, *ii*, 1297, **1344**
  - tumors, *ii*, 1300, 1387 to 1400, 1419, 1421
  - typhoid, *ii*, 1338, 1374
  - unilateral kidney, *ii*, 1293
  - uremia, *ii*, 1300, 1310, 1342, 1404
  - ureteritis, *ii*, **1418**
  - ureters, *ii*, 1297, 1405
  - uric acid, infarct, *ii*, 1375
  - urinary tubules, *ii*, 1297
  - urine, *ii*, 1317, 1325
  - varicocele, *ii*, 1401
  - vascular transformation, *ii*, **1324**
  - venous hyperemia, *ii*, 1307
  - vinylamin-poisoning, *ii*, 1315
  - visceral changes, *ii*, 1401
  - Weigerts fibrin stain, *ii*, 1306
  - weight, *ii*, 1298, 1311
  - white kidney, *ii*, **1345**, 1346, 1347, 1359, 1380
  - yellow kidney, *ii*, 1346, 1380
- Knee joint, 1244, 1251, 1259, **1263, 1270**, 1272, 1274
- Koplik spots, *i*, 549, *iii*, 2076
- Kraurosis vulvae, *ii*, 1702
- Kupffer's cells, *ii*, 1017
- Kyphosis, *i*, 368, *ii*, 1066, 1079, 1129, 1136

- Lachrymal glands, *i*, 604
- Lactation, *iii*, **1757**, 1766
- Lacunae, *ii*, 1056
- Laennec's cirrhosis, *i*, 225, *ii*, 921
- Langerhan's cells, *i*, 10, *iii*, 1712, 1745
  - islands in diabetes, *ii*, 1035
- Larynx, *i*, 305
  - abscess, *i*, 313
  - actinomycosis, *i*, 320
  - adhesions, *i*, 306
  - amyloid tumors, *i*, 323, 326
  - anatomy, *i*, 305
  - angioma, *i*, 323
  - arytenoid cartilage, *i*, 305, 313
  - ascaris, *i*, 327
  - bacteria, *i*, 309
  - branchial clefts, *ii*, **328**
  - burns, *i*, 313
  - carcinoma, *i*, 322, 324, **325, 331**
  - cartilage of Santorini, *i*, 305
  - cartilage of Wrisberg, *i*, 305
  - catarrh, *i*, **309**
  - circulation, *i*, 306
  - croup, *i*, 306
  - cysts, *i*, 306
  - diphtheria, *i*, 308, 311, 312, 319
- Larynx, edema, *i*, 308, 615
  - epiglottis, *i*, 305, **314, 318**
  - epithelioma, *i*, **322**
  - fibroma, *i*, **322**, 323
  - fistulae, *i*, 313
  - foreign bodies, *i*, 327
  - fracture, *i*, 326
  - glanders, *i*, 320
  - glands, *i*, 306
  - glottis, *i*, **307**
  - hemorrhage, *i*, 307
  - hyperemia, *i*, 307
  - infections, *i*, 308, 311
  - inflammation, *i*, 308, 318
  - influenza, *i*, 312
  - laryngitis, *i*, 310, 313, 316
  - laryngocele, *i*, 306
  - laryngotracheal bronchitis, *i*, **311**, 312
  - leprosy, *i*, 319
  - lupus, *i*, 316
  - lymphosarcoma, *i*, **324**
  - malformation, *i*, 306
  - ossification, *i*, 326
  - pachidermia, *i*, **310**
  - papillomas, *i*, 310, 320, **321**, 324
  - parasites, *i*, 327
  - perichondritis, *i*, 313, 319
  - pertussis, *i*, 309
  - phlegmon, *i*, 313, 616
  - plasma cell infiltration, *i*, 309
  - poisons, *i*, 308, 312
  - polyps, *i*, 316, **320**
  - pseudomembrane, *i*, **311**
  - pyemia, *i*, 313
  - sarcoma, *i*, 323, **324**
  - scleroma, *i*, 320
  - small pox, *i*, 319
  - smoker's catarrh, *i*, 310
  - suffocation, *i*, 321
  - syphilis, *i*, 316, **317**
  - thyroid, *i*, 324, 504, 508
  - tonsils, *i*, 606
  - trachea, *i*, 305
  - trauma, *i*, 308, 326
  - trichinosis, *i*, 327
  - tuberculosis, 314, **315**
  - tumors, *i*, 320
  - typhoid, *i*, **314**, 318
  - ulcers, *i*, **314, 317, 318**, 327
  - variola, *i*, 319
  - vocal cords, *i*, 305, 310
  - vocal cords (false), *i*, **320, 322**
- Lateral amyotrophic sclerosis, *iii*, 1995
  - spastic spinal paralysis, *iii*, 1989
- Lattice fibres, *i*, 339
- Lattice figures, *ii*, 1055
- Laveran's crescents, *i*, 208
- Lead, basophilic degener., *i*, 551
  - kidney, *ii*, 1315
  - leadline, *i*, 551
  - poisoning, *i*, 188
- Leg, artery (poplit), *i*, **105**
  - carcinoma, *i*, **169**
  - elephantiasis, *iii*, **2112, 2169**
  - ulcers, *i*, **169**, *ii*, 1106, *iii*, 2112

Leg, varices, *i*, **163**
  veins, *i*, 163
Leishman-Donovan bodies, *i*, 212, 236, *iii*, 2157
Leontiasis, *ii*, 1112
Leprosy, *iii*, **2146**
  of bone, *ii*, 1147
  intestines, *ii*, 846
  larynx, *i*, 319
  liver, *ii*, 913
  lymph nodes, *i*, 262
  mouth, *i*, 557
  nose, *i*, 299
  pharynx, *i*, 319, 620
  skin, *iii*, **2146**
  spleen, *i*, 243
  testicles, *ii*, 1493
Leptomeningitis, *iii*, 1824
Leptospira, *ii*, 1020
Leucocytes, *i*, 194
  Altmann granules, *i*, 194, 196
  basophiles, *i*, 195
  Ehrlich's granules, *i*, 194, 196
  eosinophiles, *i*, 194, 196
  eosinophilia, *i*, 195, 197
  lymphoblasts, *i*, 194
  lymphocytes, *i*, 194, 202
  lymphopenia, *i*, 198
  macrophages, *i*, 194
  mononuclears, *i*, 196, 202
  myeloblasts, *i*, 195, 202
  myelocytes, *i*, 195, 198
  plasma cells, *i*, 194, 309
  polymorphoneutrophiles, *i*, 195
Leucocytoma, *ii*, 1220
Leucocytosis, *i*, 197, 198
  lymphocytosis, *i*, 197, 198
  myelocytosis, *i*, 198
Leucoderma, *iii*, 2164, 2165
Leucopenia, *i*, 198
Leucoplakia, mouth, *i*, 553
  penis, *ii*, 1538
  tongue, *i*, 565
  urethra, *ii*, 1451
Leucosarcomatosis, *i*, 203, 279
Leukemia, *i*, 187, 188, 189, 205, 501, 805
  acute, *i*, 202
  aleukemia, *i*, 205
  bloodplatelets, *i*, 187
  bone marrow, *i*, 287
  cells, *i*, 200, 202
  intestines, *i*, 805
  kidney, *ii*, **1374**
  leucocytes, *i*, 194
  leucocytoma, *ii*, 1220
  leukemic infiltr., *i*, 203, 204
  lymphatic leukemia, *i*, 199
  lymphatics, *i*, 501
  lymphocytoma, *ii*, 1220
  lymphoma, *i*, 203
  myeloblastic leukemia, *i*, 188, 190
  myelocytes, *i*, 198
  myeloid leukemic, *i*, **263**
  normoblasts, *i*, 189
  osteosclerosis-leukemic, *i*, 204
Leukemia, peritoneum, *ii*, 872
  phagocytes, *i*, 194
  pharynx, *i*, 625
  pseudoleukemia, *i*, 205, 265
  spleen, *i*, 202, 238
  thymus, *i*, 200, 203
  tongue, *i*, 559
Leyden's crystals, *i*, 345
Lice, *i*, 213, 781, *iii*, 2090, 2155
Lichen ruber, *i*, 554, *iii*, 2100
Lids of eye, *iii*, 2025
Lieberkuehn's glands, *i*, 718
Ligaments, *ii*, 1612
  cysts, *ii*, 1554
Lightning stroke, *iii*, **2083**
Lipoiduria, *ii*, 1321
Lipoma, bone, *ii*, 1201
  intestines, *i*, 807
  kidneys, *ii*, 1391
  lipoma sarcomatodes, *iii*, **2178**
  male-breast, *iii*, **1783**
  skin, *iii*, **2177**
Lipomacia, *ii*, 1063
Lips, *i*, 545, 548
  carcinoma, *i*, 557, **567**
  cheilaschisis, *i*, 545
  cheilitis, *i*, 550
  clefts, *i*, 546
  herpes, *iii*, 2086
  macrocheilia, *i*, 177
  phlegmon, *i*, 550
  syphilis, *i*, 556
  wounds, *i*, 550
Lithocelyphopaedion, *ii*, **1610**, *iii*, 1736
Little's disease, infantile spasmod. tabes, *iii*, 1997
Littre's glands, *ii*, 1451, 1453
Littre's hernia, *i*, 734
Liver, *ii*, 883, **903**
  abscess, *ii*, **881**, 913, 915, **916**, **917**, 919
  actinomycosis, *ii*, **944**
  adenoma, *ii*, 954
  amanita, *ii*, 910
  amyloid degen., *ii*, 905, 947, **948**
  anatomy, *ii*, 883
  aneurysms, *ii*, 899
  angioma, *ii*, 852, 952
  anomalies, *ii*, 888
  artery, hepatic, *ii*, 898
  atrophy, brown, *ii*, 901
  atrophy, yellow, *ii*, 907, **909**
  bacteria, *ii*, 911
  bile, *ii*, 885, 893
  bile abscess, *ii*, 920
  bile capillaries, *ii*, 886, 978
  blood supply, *ii*, **880**
  carcinoma, *ii*, 893, **959**, **960**, **962**, **966**, **968**
  cavernous angioma, *ii*, 952
  chloroform poisoning, *ii*, 933
  circul., *ii*, 890, 894, 898
  cirrhosis, *i*, 633, *ii*, 892, **922**, **923**, **924**, **925**, **926**, **927**, 929
  cloudy swelling, *ii*, 905
  congestion, *ii*, 890
  cysts, *ii*, 955, **956**

Liver, degenerations, *ii*, 905
  diabetes, *ii*, 949
  distomum hepaticum, *ii*, 972
  echinococcus, *ii*, 971, **972, 974, 975**
  eclampsia, *ii*, **897**
  edema, *ii*, 900
  embryology, *ii*, 883
  fat infiltration, *ii*, **902**
  fatty degeneration, *ii*, 902
  focal necrosis, *ii*, **900**
  function, *i*, 195
  gall bladder, *ii*, 978
  gas edema, *iii*, **2045**
  glanders, *ii*, 945
  glycogenic infiltration, *ii*, 949
  gummas, *ii*, **938**, 939, **940, 941, 943**
  Hanot's cirrhosis, *ii*, 929
  hemorrhages, *ii*, 899
  hepatitis, *ii*, 905, 921
  hypertrophy, *ii*, 969
  icterus, *ii*, 912, 929
  infection, *ii*, 913, 946
  inflammation, *ii*, 913
  Kupffer's cells, *ii*, 1017
  Laennec's cirrhosis, *i*, 225, *ii*, 921
  leprosy, *ii*, 913
  leucocytoma, *ii*, 944
  lobulate liver, *ii*, 942
  lymphatics, *ii*, 886
  lymphogranulomatosis, *ii*, 945
  lymphoma, *ii*, 945
  malaria, *ii*, 932
  melanosarcoma, *ii*, **958**
  nerves, *ii*, 886
  nutmeg liver, *ii*, 891
  occlusions, *ii*, 893, 895
  parasites, *ii*, 921, 971
  periportal infection, *ii*, **918**
  phlebitis, *ii*, 893
  phosphorus-poisoning, *ii*, 912
  pigment, *ii*, 926
  pigment infiltration, *ii*, 950
  poisons, *ii*, 906, 907, 910, 912, 913, 931, 933
  portal vein, *i*, 100, 158, *ii*, 894, **917**
  position changes, *ii*, 890
  postmortem changes, *ii*, 887
  regeneration, *ii*, **892**, 969
  renal ptosis, *ii*, 1299
  rupture, *ii*, **899**
  sarcoma, *i*, 257, *ii*, 957, **958**
  suppuration, *ii*, 919
  syphilis, *ii*, **937, 940, 941, 942**
  thrombophlebitis, *ii*, 893, **919**
  toadstool-poisoning, *ii*, 906, 910, 913
  tropical abscess, *ii*, 915
  tuberculosis, *ii*, **934, 935**
  tumors, *ii*, 952 to 957
  vein, hepatic, *ii*, 893, 895
  weight, *ii*, 887
  Wilson's disease, *ii*, 954, **970**
Liver diet for pernicious anemia, *i*, 191
Livor, *iii*, 2068
Lochia, *iii*, 1717
Lordosis, *ii*, 1079, 1163, 1264

Louse, typhus etc., *i*, 782
Ludwig's angina, *i*, 595
Lumbar puncture, *iii*, 1830
Lungs, *i*, 292, 358
  abscess, *i*, 155, 404, 410, 411, 414
  absorption atelectasis, *i*, 361
  actinomycosis, *i*, 466, **467**
  air contents, *i*, 359
  anemia, *i*, 370, 388
  aneurysms, *i*, 145
  anthracosis, *i*, 372, 418, 420, **474**
  asphyxia, *i*, 382
  aspiration pneumonia, *i*, 406, 414
  atelectasis, *i*, 359
  bacteria, *i*, 386, 389, 406, 428
  blood pigment, *i*, 371
  bronchopneumonia, *i*, 362, 401, 402, **403**, 407
  carcinoma, *i*, 378, 470, **478**
  carnification, *i*, **399**
  caseation, *i*, 408, 437
  chalicosis, *i*, 421
  chorionepithelioma, *i*, 475, **477**
  circulation, *i*, 370, 380
  coal pigment, *i*, 372, 418, 420, 474
  cold abscess, *i*, 404
  collapse, *i*, 359, 362
  compression atelectasis, *i*, 361
  congestion, passive, *i*, 372, 375
  death by drowning, *i*, 155, 413
  death sudden, *i*, 383
  distension, *i*, 363
  distomum pulmonale, *i*, 481
  echinococcus, *i*, 481
  edema, *i*, 374, 377
  emboli, *i*, 155, **365, 367**, 381, **383**, 388, 398, 413
  emphysema, *i*, 363
  fat emboli, *i*, 376, 386, **387**
  fetal lung, *i*, 360
  foreign body pneumonia, *i*, 406
  gangrene, *i*, 400, 402, **409**, 411
  giant cells, *i*, 423
  glanders, *i*, 465
  gummas, *i*, **465**
  hemorrhage, *i*, 371, 373, 377
  hepatization, *i*, 392
  hernia, *i*, 368
  hyperemia, *i*, 370
  hypertrophy, *i*, 373
  hypostatic hyperemia, *i*, 358, 373
  induration, *i*, **373**, 398, 412
  infarction, *i*, 379, **383**, 384
  infection, *i*, 386, 389
  inflammation, *i*, 389
  influenza, *i*, 389, 403
  lymphatics, *i*, 174, 397
  malformation, *i*, 359
  metastases, *i*, 391
  mixed infection, *i*, 389, 427, 447
  occlusion of pulmon. artery, *i*, 381
  parasites, *i*, 480, 481
  pest pneumonia, *i*, 406
  pigment emboli, *i*, 388
  pigments, *i*, 371, 421

Lungs, plague, *i*, 406
  pneumococcus, *i*, 389, **394**
  pneumoconiosis, *i*, 418, 420
  pneumomalacia, *i*, 414
  pneumomycosis, *i*, 480
  pneumonia acute, *i*, 414
  pneum. caseous, *i*, 408, 437
  pneum. croupous, *i*, 389, **416,** 417
  pneum. fibrinous, *i*, 388
  pneum. fr. foreign bodies, *i*, 417
  pneum. interstit., *i*, **391, 393, 394,** 414
  pneum. lobar, *i*, 388, 398
  pneum. lobular, *i*, 398, **407**
  pneum. migrans., *i*, 396
  pneum. purulent, *i*, 400
  pneum. septic of new born, *i*, 414
  pneum. smooth, *i*, 440
  pneum. tuberculous, *i*, 425, 428, 437
  postmortem changes, *i*, 358
  psittacosis, *i*, 406
  pulmonary artery, *i*, 381
  pulmon. distension, *i*, 363
  pulmonary lymphangitis, *i*, 399
  resolution, *i*, 395
  respiratory organs, *i*, 292
  sarcoma, *i*, 475, **479**
  siderosis, *i*, 422
  spirillum sputigenum, *i*, 411
  splenization, *i*, 362
  syphilis, *i*, 461, 462, **464, 465**
  syphilis, congenital, *i*, 462
  trauma, *i*, 369, 378
  tubercle bacilli, *i*, 43, 419
  tuberculosis, *i*, 349, 378, 422, 428, 435, 444
  tuberculosis, miliary, *i*, 430, **432, 438, 439**
  tumors, *i*, 469
  tumors circumscribed, *i*, 473
  tumors metastatic, *i*, 475
  war gas, *i*, 376, 377
Lupus, erythematous, *iii*, 2122
  of hand, *iii*, **2122, 2123**
  of larynx, *i*, 316
  of mouth, *i*, 555
  of nose, *i*, 297
  of pharynx, *i*, 620
  of tongue, *i*, 555
Luschka's ducts, *ii*, 979, 997
Lutein cells, *ii*, 1480, 1618
Luxation, *ii*, 1268
Lymph, *i*, 185, 215, 216
  lymphadenocystoma, *i*, 175
  lymphadenopathy, *i*, 267
  lymphadenosis, *i*, 265, 266
  lymphangioectasis, *i*, 175
  lymphangioendothelioma, *i*, 170
  lymphangioma, *i*, 177, **247,** 502, *ii*, 1201
  lymphangitis, *i*, 173, 340, 399
  lymphangitis, puerperal, *ii*, 1606
Lymph nodes, *i*, 248
    abscesses, *i*, 252
    adenocarcinoma, *i*, **283**
    adeny aleukemic, *i*, 265
    amyloid degenerat., *i*, 285
    anatomy, *i*, **248**
    anthracosis, *i*, 250, 254
Lymph nodes, anthrax, *i*, 252
    atrophy, *i*, 284
    bacteria, *i*, 258
    blastomas, *i*, 266
    blood pigment, *i*, 254
    blood vessels, *i*, 249
    bubo, *i*, 252, *ii*, 1534
    bubonic plague, *i*, 252
    calcification, *i*, 258, 285
    carcinoma, *i*, 184, 282, **283**
    caseation, *i*, 257
    cervical, *i*, 258
    chancre, *i*, 252
    chloroma, *i*, 272, **273**
    chrysops, *i*, 262
    circulation, *i*, 249
    degeneration, *i*, 284, 285
    dermacentor, *i*, 262
    diseases, *i*, 250
    echinococcus, *i*, 285
    fatty degeneration, *i*, 285
    functions, *i*, 249
    germinal center, *i*, 249
    glanders, *i*, 252
    hemolymph nodes, *i*, 250
    hemorrhages, *i*, 254
    Hodgkin's disease, *i*, 266, 271
    hyalin degen., *i*, 285
    hyperplasia, *i*, 253, 263
    infect. granulom. tumors, *i*, 255
    inflammation, *i*, 253
    leprosy, *i*, 262
    leukemic lymphoma, *i*, 236
    lipomatosis, *i*, 284
    liquefaction ichorous, *i*, 253
    lymphadenitis, *i*, 251, 253, 259
    lymphadenopathy, *i*, 267
    lymphadenosis, *i*, 265, 266
    lymphogranulomatosis, *i*, 258, 267, 270
    lymphoma, *i*, **263, 264**
    lymphoma, aleukemic, *i*, 277
    lymphomatosis, *i*, 264, **269**
    lymphosarcoma, *i*, 174, 274, 275, 276, 278, 279, 282
    mediastinal tumor, *i*, 280
    myeloid metamorphosis, *i*, 263
    necrosis, *i*, 252
    Ohara's disease, *i*, 262
    ossification, *i*, 285
    parasites, *i*, 285
    physiology, *i*, 249
    pigmentation, *i*, 254
    plague, bubonic, *i*, 252
    plasmacytoma, *i*, 276
    pneumonia in children, *i*, 260
    pseudoleukemia, *i*, 265
    reticulo-endothelial apparatus, *i*, 250
    rupture, *i*, 260
    sarcoma, *i*, 281, **282**
    suppuration, *i*, 253
    supraclavicul. gl., *i*, 184
    syphilis, *i*, 261
    tattooing, *i*, 254
    trichinae, *i*, 285
    tuberculosis, *i*, **255, 257**

Heavy face type denotes an illustration.

Lymph nodes, tularemia, *i*, 262
  tumor, *i*, 270
  woodtick, *i*, 212
Lymph spaces, *i*, 172
Lymph vessels, *i*, 167, 172
  anthracosis, *i*, 174
  ascites, chylous, *i*, 176
  bacteria, *i*, 173
  brain, *i*, 181
  bronchi, *i*, 340
  carcinoma, *i*, 175, 177, 179
  cavities, *i*, 175
  chylothorax, *i*, 176
  coriocarcinoma, *i*, 181
  cylindroma, *i*, 182
  cysts, *i*, 177
  dura, *i*, 181
  elephantiasis, *i*, 176, 210
  enchondroma, *i*, 184
  endolymphangitis, *i*, 174
  endothelial psammoma, *i*, 181
  endothelial sarcoma, *i*, 182
  endothelioma, *i*, 178, 183
  fat embolism, *i*, 208
  filaria, *i*, 210
  giant cells, *i*, 180
  glanders, *i*, 175
  gonorrhea, *i*, 173
  hygroma, *i*, **178**
  hyperplasia, *i*, 176
  infections, *i*, 175
  inflammations, *i*, 173
  intestines, *i*, 718
  leucopenia, *i*, 198
  leukemia, *i*, 501
  leukemic infiltration, *i*, 204
  leukemic lymphoma, *i*, 203
  leukocytosis, *i*, 197
  liver, *ii*, 886
  lungs, *i*, 397
  lymph, *i*, 185, 215
  lymph capillaries, *i*, 172
  lymph sheaths, *i*, 104
  lymph spaces, *i*, 172
  lymphadenocystoma, *i*, 175
  lymphangiectasis, *i*, 175
  lymphangioma, *i*, 177
  lymphangitis, *i*, 173
  lymphoma, *ii*, 945
  lymphopenia, *i*, 187
  lymphorrhagia, *i*, 176
  lymphosarcoma, *i*, 174, 179
  metabolism, *i*, 215
  metastases, *i*, 179, 185
  myelocytosis, *i*, 188
  nevi-cellulae, *i*, 182
  pachydermia, *i*, 310
  parasites, *i*, 184
  parotid, *i*, 181
  perilymphangitis, *i*, 174
  perithelioma, *i*, 178
  peritoneum, *ii*, 881
  Peyer's patches, *i*, 718
  phlegmons, *i*, 174
  pigment, *i*, 216,
Lymph vessels, prostate, *i*, 175
  pyemia, *i*, 174
  rupture, *i*, 176
  salivary glands, *i*, 181
  sarcoma, *iii*, 1791
  spleen, *i*, 218
  stasis, *i*, 176
  syphilis, *i*, 175
  thoracic duct, *i*, 172, 176
  thrombolymphangitis, *i*, 174
  thymus, *i*, 200
  tuberculosis, *i*, 174
  tumors, *i*, 174, 177, 178, **180**, **182**, 183
  varicosities, *i*, 177
Lymphatics, elephantiasis, *i*, 176
  endothelium, *i*, 180
  hygroma, *i*, 177
  lymphangioma, *iii*, **2185**, **2186**, **2187**
Lymphoblasts, *i*, 194
Lymphocytes, *i*, 194
Lymphocytoma, *ii*, 1020
Lymphogranulomatosis, *i*, **264**, 267
  liver, *ii*, 945
  pharynx, *i*, 624
  spleen, *i*, 239
  stomach, *i*, 672
Lymphoid marrow, *i*, 287
Lymphoma, *i*, **263**, 264
Lymphomatosis, *i*, 174, **269**
Lymphopenia, *i*, 187
Lymphorrhagia, *i*, 176
Lymphosarcoma, *i*, 174, 179, 274, **275**, **278**
  larynx, *i*, **324**
  pleura, *i*, 495

MACROCEPHALY, *ii*, 1189
Macrocheilia, *i*, 177, 562
Macroglossia, *i*, 177, 562
Macromastia, *iii*, 1770
Macrosomia, *ii*, 1186
Macrostomia, *i*, 546
Maidism, (pellagra), *iii*, 2002
Malakoplakia, *ii*, 1428
Malaria, *i*, **209**
  anopheles, *i*, 208
  blood changes, *i*, 190
  brain, *iii*, 1919
  liver, *ii*, 932
  malaria granuloma, *iii*, 1919
  melanin, *i*, 210
  melanuria, *i*, 210
  plasmodia, *i*, 208
  spleen, *i*, 235
Malformations, bladder, *ii*, 1422
  bone, *ii*, 1065, 1072, 1079
  brain, *i*, 142, *iii*, **1807**, **1883**, **1885**, **1887**
  esophagus, *i*, **630**, **631**
  gall bladder, *ii*, 979
  heart, *i*, 1, 28, 47, 86, 89
  intestines, *i*, 719
  kidney, *ii*, 1296
  larynx, *i*, 306
  lips, *i*, 545
  liver, *ii*, 888
  lungs, *i*, 359

Malformations, mouth, *i*, 544
  nose, *i*, 292
  pancreas, *ii*, 1021
  pelvis, *ii*, 1078
  pericardium, *i*, 1, 6
  sex organs, *ii*, 1466, **1481**, **1483**
  skull, *ii*, 1165, 1188, 1189
  spleen, *i*, 220
  stomach, *i*, 660
  teeth, *i*, 584
  thyroid, *i*, 506
  tongue, *i*, 562
  ureters, *ii*, 1296
  urethra, *ii*, 1424, 1448
Malpighian corpuscles, *i*, 216
Mast cells, *i*, 10, 195
Mastitis, *iii*, 1761, **1764**, 1767
Maxilla, actinomycosis, *i*, **558**
  adamantinoma, *i*, 585, **589**, **590**
  central fibroma, *i*, **592**
  clefts, *i*, 329, *ii*, **928**
  cysts, *i*, 586
  osteosarcoma, *ii*, **1210**
  phosphorus necrosis, *ii*, **1121**
  in rachitis, *ii*, 1165
  tumors, *i*, **592**
Maxillary sinuses, *i*, 296
Measles, *iii*, 2075
  Koplik's spots, *iii*, 2076
Meat poisoning, *i*, 762, *iii*, 2080
Meckel's, diverticulum, *i*, 725, 748
Meconium, *i*, 719, *ii*, 859
  in lungs, *i*, 360, 413
Mediastinum, *i*, 503
  congenital cysts, *i*, 503
  echinococcus, cysts, *i*, 505
  goiter, substernal, *i*, 501
  lymphangiomas, *i*, 502
  mediastinal pericarditis, *i*, 5
  sarcomas, *i*, 503
  teratoma, *i*, 504
  thoracic duct, *i*, 172
  thymus tumors, *i*, 495
  tuberculosis, *i*, 503
  tumors *i* 280 504
Medulla oblongata, *iii*, 1834
Megacaryocytes, *i*, 187, 286
Meissner's plexus, *i*, 719
Melanemia, *i*, 204
Melanin, *i*, 210, *ii*, 1260
  adrenals, *ii*, 1277
Melanoma, *iii*, 1843
Melanoplakia, *i*, 553, *ii*, 1283
Melanosarcoma, *i*, 246, *iii*, **2193**, **2194**
Melanosis, *i*, 759, 804
Melanuria, *i*, 210
Melenia, *i*, 663
Meloschisis, *i*, 546
Meningitis, *iii*, 1824, 1828
  epidemic cerebrospinal, *iii*, 1830
  hydrocephalic, *iii*, 1823, 1832
  idiopathic, *iii*, 1829
  meningococcus, *iii*, 1830
  serous, *iii*, 1825
  suppurative, *iii*, 1825
Meningitis, syphilitic, *iii*, 1864
  tuberculous, *i*, 131, *iii*, 1815, 1832, 1837
Meninges, *iii*, 1804, 1810, 1824, 1852
  abscess, *iii*, 1828
  actinomycosis, *iii*, 1815, 1837
  anatomy, *iii*, 1804
  arachnoidea, *iii*, 1804, 1855
  bacteria, *iii*, 1809, 1827, 1830, 1832
  brain sand, *iii*, 1841
  cerebrospinal fluid, *iii*, 1805
  cerebrospinal meningitis, *iii*, 1830
  cholesteatomas, *iii*, 1839, **1840**
  choroid plexus, *iii*, **1817**, 1834, 1841
  circulation, *iii*, 1806
  cysterna magna, *iii*, 1805
  cysticercus, *iii*, 1845
  cysts, *iii*, 1838, 1841
  dura, *iii*, 1804, 1809, **1814**
  edema, *iii*, 1823
  epidemic cerebrospinal meningitis, *iii*, 1830
  fibroendothelioma, *iii*, **1818**
  glioma, *iii*, **1842**, 1930
  hematoma, *iii*, 1809, **1813**
  hemorrhage, *iii*, **1807**, 1809, 1823, 1943
  hygroma of dura, *iii*, **1814**
  inflammation, *iii*, 1824, 1830, 1831
  leptomeningitis, *iii*, 1824
  leukemic infiltrates, *iii*, 1815
  lumbar puncture, *iii*, 1830
  medulla oblongata, *iii*, 1843
  melanoma, *iii*, 1843
  meningitis, *iii*, 1824, 1825, 1830, 1835, 1836, 1837
  meningococcus, *iii*, 1830
  osteoma, *iii*, **1821**
  otitis media, *i*, 295, *iii*, **1826**, **1828**
  Pacchionian bodies, *iii*, 1805
  pachymeningitis, *iii*, 1811, 1814
  parasites, *iii*, 1837, **1845**
  pia, *iii*, 1805, 1824, 1860
  pia-arachnoidea, *iii*, 1822, 1838
  post mortem findings, *iii*, 1810, 1822
  psammoma, *iii*, **1816**, **1817**, 1818, **1820**, **1821**
  sarcoma, *iii*, 1819, **1820**, **1822**, 1844, 1932, **1966**
  spinal meninges, *iii*, 1822
  spinal meningitis, *iii*, 1959
  subarachnoidal space, *iii*, 1855
  subdural hemorrhage, *iii*, 1809
  suppurative meningitis, *iii*, 1825
  syphilis, *iii*, 1815, 1816
  telachorioidea, *iii*, 1805, 1837
  thrombosis, *iii*, 1806, 1808, 1809
  trauma, *iii*, 1810, 1811, 1812, 1828
  tuberculosis, *iii*, 1815, 1832, 1833, **1835**, **1836**, 1837
  tumors, *iii*, **1814**, 1816, **1818**, **1820**, **1821**, **1822**, 1837, 1838, 1840, 1841, **1842**, 1843, 1932, **1966**
  ventricles, *iii*, 1805, 1846
Menorrhagia, *ii*, 1620
Menstruation, *ii*, 1618
  corpus luteum, *ii*, 1618
  menstrual cycle, *ii*, 1618

- Menstruation, menstrual poisoning, *ii*, 1618
- Mercury poisoning, intestines, *i*, 770
  - kidney, *ii*, 1302, **1379**
  - ptyalism, *i*, 551
  - stomatitis, *i*, 551
- Merozoids, *i*, 209, 239
- Mesaortitis, *i*, 127, 137
- Mesarteritis, *i*, 121
- Mesentery, *ii*, **879**
- Metabolism, *i*, 219
  - and arteriosclerosis, *i*, 115
  - cholesterin, *i*, 220
  - hemoglobin, *i*, 220
  - of iron, *i*, 219
- Metaplasia of bone, *ii*, 1061, 1084
  - lymphatics, *i*, 174, 177, 178, 183
  - myeloid, *i*, 191, 263
- Methemoglobin, *i*, 187
- Metritis, *ii*, 1623, *iii*, 1641, **1660**
- Metrolymphangitis, *iii*, 1753
- Metrophlebitis, *iii*, 1752
- Metrorrhagia, *ii*, 1622
- Microcephalia, *iii*, 1853, **1856, 1857**
- Microcytes, *i*, 188, *ii*, 1189
- Microdactylia, *iii*, 2053
- Microgametes, *i*, 209
- Micrognathia, *ii*, 1170
- Microgyria, *iii*, 1858
- Micromastia, *iii*, 1759
- Micromelia, *ii*, 1169, **1170, 1178**
- Microsporia, *iii*, 2151
- Microstomia, *i*, 544
- Miescher's tubes (trichinosis), *iii*, **2060**
- Mikulicz's cells (rhinoscleroma), *i*, 300
  - Mikulicz's disease, *i*, 604
- Miliaria, (prickly heat), *iii*, 2085
- Miliary aneurysms, *i*, 141
  - tuberculosis, *i*, **432**
- Milium (mouth), *i*, 549
- Milk, *iii*, **1757**, 1759
  - colostrum, *iii*, 1758
  - lactation, *iii*, **1757**
  - male breast, *iii*, **1758**
  - newborn, *iii*, **1758**
- Milk spots, *i*, **13**
- Milk teeth, *i*, **582**
- Mitral lesions, *i*, **34, 40**, 43
- Mitral stenosis and brown induration of lung, *i*, **373**
- Mixed tumor of parotid, *i*, 593, 597
- Moeller-Barlow's scurvy in childhood, *ii*, 1166, 1167, **1168**
- Mole formation, blood mole, *i*, 171, *iii*, 1736
  - hydatiform m., *iii*, 1698, **1722**, 1724, **1725**, 1727
  - in testes, *iii*, 1746
- Molluscum contagiosum, *iii*, **2156**, 2157
- Mongolism, *i*, 526
- Montgomery's glands (nipple), *iii*, 1759
- Morbilli, (measles), *iii*, 2075
- Morgagni's hydatid cysts, *ii*, 1464, 1590
- Morvan's disease of spinal cord, *iii*, 1981
- Mosquitoes, anopheles (malaria), *i*, 208
  - of yellow fever, stegomyia, *ii*, 1020
- Mouth, *i*, 543
- Mueller's ducts, *ii*, **1458**, 1460, 1462, 1464
- Mumps, *i*, 593
  - and testes, *i*, 594
- Muscles, *iii*, 2032
  - abscess, *iii*, 2041, 2048
  - actinomycosis, *iii*, 2049
  - amyloid changes, *iii*, 2039
  - amyotrophic atrophy, *iii*, 2035
  - anatomic changes, *iii*, 2035
  - anatomy, *iii*, 2032
  - anemia, *iii*, 2048
  - atrophy, *iii*, 1997, 2035
  - bacteria, *iii*, 2042
  - calcification, *iii*, 2039
  - carcinoma, *iii*, 2055
  - circulation, *iii*, 2034
  - congenital defects, *iii*, 2034
  - cysticercus, *iii*, **2060**
  - degenerat., *iii*, 2034, **2037**
  - dystrophy, *iii*, 2035, 2049
  - echinococcus, *iii*, 2061
  - emphysema, *iii*, 2042
  - eosinophilia, *iii*, 2060
  - gas phlegmons, *iii*, **2042, 2043**
  - glanders, *iii*, 2048
  - heart, *i*, 66, *iii*, 2042
  - hematoma, *iii*, 2034
  - hemophilia, *iii*, 2034
  - hemorrhage, *iii*, 2034
  - hypertrophy, *iii*, 2035, 2049
  - inflammations, *iii*, 2039
  - lipodistrophy, *iii*, 2035
  - lipomatosis, *iii*, 2049
  - Miescher's tubules, *iii*, **2060**
  - myopathy, *iii*, 2035
  - myositis, *i*, 39, *iii*, **2041**, 2045, 2051, 2052
  - myotonia, *iii*, 1997, 2049, 2050
  - neuroma, *iii*, **2029**
  - neuropathic atrophy, *iii*, 2035
  - ossification, 2052, **2053**
  - parasites, *iii*, 2056
  - phlegmons, *iii*, **2042**
  - phosphorus poisoning, *iii*, 2034, 2037
  - pigment, *iii*, 2034
  - poliomyelitis, *iii*, 1990
  - polymyositis, *iii*, 2040
  - post mortem changes, *iii*, 2033
  - pseudo hypertrophy, *iii*, 2036
  - regeneration, *iii*, 2050
  - rhabdomyoma, *iii*, 2055
  - rheumatic myositis, *iii*, 2040
  - sarcoma, *iii*, 2055
  - suppuration, *iii*, **2041**
  - syphilis, *iii*, 2046, **2047**
  - Thomsen's myotonia, *iii*, 2049
  - trauma, *iii*, 2039, 2045
  - trichinae, *iii*, 2040, **2056, 2057, 2060**
  - tuberculosis, *iii*, 2040, 2046
  - tumors, *iii*, 2055
  - waxy degenerat., *iii*, **2037**
  - wry neck, *iii*, 2045
- Mushroom poisoning, *ii*, 910, 1013
  - liver, *ii*, 906, 910, 913
- Mycosis fungoides, *iii*, 2153
- Myeloblasts, *i*, 194

Heavy face type denotes an illustration.

Myeloclasts, *iii*, 2034
Myelocytes, *i*, 190, 198, 286
Myelocytocele, *iii*, 1974
Myelocytoma, *ii*, **1219**
Myelocytosis, *i*, 188
Myeloid chloroma, *i*, **273**
Myeloid metaplasia, *i*, 191, 263
Myelomalacia, *ii*, 1130
Myelomas, *ii*, **1218**
Myelomeningocele, *iii*, 1974
Myeloplaxes, *iii*, 2064
Myelosis, *i*, 286
Myiasis, *i*, 305
Myocardium, *i*, 48
  anatomy, *i*, 48
  anemic infarcts, *i*, 58
  atrophy, *i*, 49
  Buhl's disease (newborn), *i*, 53
  calcification, *i*, 23, 24
  coronary vessels, *i*, 55, 56
  degenerat., *i*, 22, 23, 51, 61
  diphtheria, *i*, 61
  fragmentation, *i*, 70
  infarcts, *i*, 58, 59
  ischemia, *i*, 21, 58
  myocarditis, *i*, 6, 58, 60, 63
  pigment, *i*, 49
  rupture, *i*, 54, 69
  scars, *i*, 67
  segmentation, *i*, 70
  syphilis, *i*, 17, 82
  tuberculosis, *i*, 17, 82
  Winkel's disease, *i*, 53
Myoma, *iii*, 1646
  intestinal, *ii*, 806
Myositis, fibrous, *iii*, 2045
  ossificans, *iii*, 2051, 2052
  suppurative, *iii*, **2041**
Myotonia, congenit. (Thomsen's disease), *iii* 1997, 2049, 2050
Myxedema, *i*, 529
Myxoma, of bone, *ii*, 1220
  nose, *i*, 301
Myxosarcoma, *iii*, **2191**
  peritoneum, *ii*, **873**

Naegeli's pelvis, *ii*, 1188
Nails, *iii*, 2223
  exostoses, *iii*, 2224
  fungi, *iii*, 2149, 2150
  ingrown, *iii*, 2224
  leuconychia, *iii*, 2224
  onychia syphilit., *iii*, 2223
  onychogriphosis, *iii*, 2223, **2224**
  paronychia, *iii*, 2223
  psoriasis, *iii*, 2224
  scarlet fever line, *iii*, 2076
  tumors, *iii*, 2224
Nannosomia, *ii*, 1179, 1180
Nearthroses, *ii*, 1086, 1089
Necrosis, *ii*, 1062
  bone, *ii*, 1116, **1117, 1118, 1119**
  kidney, *ii*, 1302, 1305, 1310, **1324**
  lymph nodes, *i*, 252
  pancreas, *ii*, 1024, 1026
Necrosis, phosphorus, *ii*, **1121**
  sequestrum, *ii*, 1118
  symmetr. gangrene, *iii*, 2110, 2147
Negri bodies in rabies, *iii*, 1900
  ganglion cells in hippocampus major, *iii*, 1901
Nematodes—roundworms, *ii*, 852
Nephrectomy, *ii*, 1416
Nephritis, *ii*, 1320, 1329, 1332, 1338, 1339
  diphtheria, *ii*, **1329**
  embolic, focal, *ii*, **1336**
  glomeruli, *ii*, **1329, 1330, 1336, 1342, 1343**
  heart, *i*, 2, 15, 38, 56
  hematogenous, *ii*, 1338
  interstitial, *ii*, 1331
  pyelonephritis, *ii*, **1363**
  scarlet, *ii*, **1329**, 1330, 1333, 1334, 1342, 1343
  suppurative, *ii*, 1339
Nephrolithiasis, *ii*, 1377
Nephropexy, *ii*, 1299
Nephroptosis, *ii*, 1298
Nephrosis, *ii*, 1317, **1411, 1412**
Nervous system, *iii*, 1804, 1809
    adrenals, *ii*, 1277
    amputation neuromas, *iii*, 2014, 2021
    amyotrophic fibroma, *iii*, **2022**
    amyotroph. lat. sclerosis, *iii*, **1995**
    arteries, *i*, 100
    atrophy, *iii*, 2014
    beri-beri, *iii*, 2016
    bone atrophy, *ii*, 1070
    bone marrow, *i*, 282
    brain, *iii*, 1852
    bronchi, *i*, 339
    carcinoma, *iii*, **2031**
    chromaffin cells, *ii*, 1277
    chromatophores, *iii*, 1843
    compression, *i*, 139
    degeneration, *iii*, 2013, 2015
    fibroma, *iii*, **2022**
    ganglion neuroma, *iii*, **2023**
    heart, *i*, 20
    infection, *iii*, 2016
    inflammation, *iii*, 2013, 2016
    lead poison, *iii*, 2017
    leprosy, *iii*, 2018
    liver, *ii*, 886
    medulla, *iii*, 1843
    melanoma, *iii*, 1843
    neurinoma, *iii*, **2027**
    neuritis, *iii*, 2015, 2018
    neuroblastoma, *ii*, 1288
    neurofibromatosis, *iii*, **2024, 2026, 2027**
    neuromas, *i*, 492, *iii*, 1931, 2014, 2021, 2023
    neuron. elephantiasis, *iii*, 2026
    neuropathic arthropathy, *ii*, 1250
    neuroses, *iii*, 1942, 2099
    olfactory n., *i*, 292
    optic, *iii*, 2015
    peripheral, *iii*, 2013
    poisons, *iii*, 2017
    puerperal neuritis, *iii*, 2018
    Raynauds d., *iii*, 2110, 2147

Heavy face type denotes an illustration.

- Nervous system, v. Recklingshausen's dis., *iii*, 2027
  - sarcoma, *iii*, 2031
  - spinal n., *iii*, **1960,** 1963, 1968
  - syphilis, *iii*, 2018
  - trauma, *iii*, 2014, 2015, 2018
  - tuberculosis, *iii*, 2018
  - tumors, *iii*, **1842,** 1936, 1963, 2014, 2021, **2023, 2031**
- Neuroses, *iii*, 1942, 2099
- Nevi, *i*, 171, 182, *iii*, **2173, 2187**
  - of face, *iii*, **2181, 2182, 2183**
  - lymphatic, *i*, 182
- Nipple, *iii*, 1756, 1761, 1787
  - Montgomery's glands, *iii*, 1759
  - Paget's dis., *iii*, 1787
  - polythelia, *iii*, 1759
  - thelitis, *iii*, 1761
- Noma, *i*, **552**
- Normoblasts, *i*, 287
- Nose, *i*, 292
  - accessory cavities, *i*, 295, 297
  - adenoids, *i*, 301
  - antrum of Highmore, *i*, 295
  - atrophy of mucosa, *i*, 295
  - bacteria, *i*, 293, 295, 299
  - carcinoma, *i*, 304, *iii*, **2202**
  - catarrh, *i*, 293, 294
  - chrome ulcers, *i*, 297
  - circulation, *i*, 292
  - cold, *i*, 293, 294
  - coryza, *i*, 293
  - diphtheria, *i*, 294
  - epistaxis, *i*, 293
  - Eustachian tubes, *i*, 295
  - glanders, *i*, 298
  - granuloma, *i*, 297
  - hayfever, *i*, 293, 344
  - hemorrhage, *i*, 293
  - infections, *i*, 293
  - inflammations, *i*, 293
  - influenza, *i*, 296
  - leprosy, *i*, 299
  - lupus, *i*, 297
  - malformations, *i*, 292
  - maxillary sinuses, *i*, 296
  - meningitis, *i*, 295
  - Mikulicz's cells, *i*, 300
  - mucosal hyperplasia, *i*, 294, 301
  - myxoma, *i*, 301
  - olfactory nerve, *i*, 292
  - operations, *i*, 296
  - ozena, *i*, 295
  - parasites, *i*, 304
  - poisons, *i*, 293
  - pollen irritation, *i*, 293
  - polyps, *i*, 296, 301, **302**
  - pseudomembranes, *i*, 294
  - purulent catarrh, *i*, 294
  - rhinitis, *i*, 293, 294
  - rhinoliths, *i*, 304
  - rhinoscleroma, *i*, 300
  - rhinophyma, *iii*, **2105**
  - Rissel bodies, *i*, 300
  - sarcoma, *i*, 303
- Nose, scrofulous children, *i*, 260
  - secretions, *i*, 293, 295
  - septum, *i*, 297
  - sinuses, *i*, 296
  - syphilis, *i*, 295, 298
  - trauma, *i*, 296, 297
  - tuberculosis, *i*, 295, 297
  - tumors, *i*, 293, 301, 304
  - turbinates, *i*, 293, 295
  - ulcers, *i*, 297
- Nutmeg liver, *ii*, 891

- OBESITY, adiposis dolorosa, *iii*, 2179
- Ochronosis, *ii*, 1230
- Odontoma, *i*, 585
- Ohara's Japanese form of tularemia, *i*, 262
- Oidium albicans (thrush, aphthae) breast, *i*, **561**
  - mouth, *i*, 549, 560
  - tongue, *i*, 560
  - vagina, *iii*, 1698
- Oligocythemia, *i*, 185, 187
- Oligohydramnion, *iii*, 1721
- Oligohydremia, *ii*, 1270
- Oliguria, *ii*, 1319, 1340
- Omentum, *i*, 747
  - omentitis, *ii*, 869, 875
- Onychia, *iii*, 2223
- Onychogryphosis, *iii*, **2224**
- Onychomycosis, *iii*, 2224
- Oophoritis, *ii*, 1548
- Oozytes, *iii*, 209
- Ophthalmia, *ii*, 1453
- Optic nerve, *iii*, 2015
- Oral cavity, *i*, 543, 571
  - abscess, *i*, **616**
  - actinomycosis, *i*, 557
  - ameba, *i*, 560
  - amyloid tumor, *i*, 564
  - anatomy, *i*, 543
  - angina, Vincent's, *i*, 550, 560
  - aphthous stomatitis, *i*, 549
  - bacteria, *i*, 550, 553, 559
  - basophilic degeneration, *i*, 551
  - Bednar's aphthae, *i*, 549
  - Blandin-Nuhn gland, *i*, 575
  - Bochdalec's tubes, *i*, 574
  - branchiogenetic cysts, *i*, 576
  - carcin. of cheek, *i*, 556, 572
  - carc. of gums, *i*, 572
  - carc. of lips, *i*, 566
  - carc. of tongue, *i*, 556, 568
  - catarrhal stomatitis, *i*, 548
  - cheilitis, *i*, 548
  - copper poisoning, *i*, 550
  - cysticercus, *i*, 576
  - cysts, *i*, 574
  - dermoid cysts, *i*, 575
  - diphtheria, *i*, 560, **611**
  - echinococcus, *i*, 576
  - embryology, *i*, 543
  - epidemic stomatitis, *i*, 550
  - epulis, *i*, 573
  - erythema, *i*, 548, 556
  - fungiform papillae, *i*, 563

Heavy face type denotes an illustration.

- Oral cavity, gangrene, *i*, 551
  - geographical tongue, *i*, 554
  - giant cell sarcoma, *i*, 573
  - gingivitis, *i*, 548
  - glanders, *i*, 559
  - glands, *i*, 507, 575, 593
  - glossitis, *i*, 548
  - gonorrhea, *i*, 548
  - gumma, *i*, 556
  - gums, *i*, 573
  - harelip, *i*, 545
  - inflammation, *i*, 548
  - Koplic's spots, *i*, 549
  - lead poison, *i*, 551
  - leprosy, *i*, 557
  - leukemic stomatitis, *i*, 553, 559
  - leukoplakia, *i*, 553
  - lichen ruber, *i*, 554
  - lip, *i*, 545, 548
  - lupus, *i*, 555
  - macrocheilia, *i*, 562
  - macroglossia, *i*, 562
  - malformations, *i*, 544
  - measles, *i*, 549
  - melanoplakia, *i*, 553
  - mercurial stomatitis, *i*, 551
  - milia, *i*, 549
  - noma, *i*, 552
  - oidium albicans, *i*, 549, 560
  - palate, *i*, 545, 557, **611**
  - papilloma, *i*, 565
  - parotid gland, *i*, 593
  - pharynx, *i*, 604
  - phlegmonous stomatitis, *i*, 550
  - phosphorous poisoning, *i*, 550
  - plasma cells, *i*, 55
  - plasmocystoma, *i*, 564
  - poisons, *i*, 550, 551, 628
  - pseudomembranous stomatitis, *i*, 549, 608, 614
  - ptyalism, *i*, 551
  - ranula, *i*, 507, 574
  - rhabdomyoma, *i*, 572
  - rhagades, *i*, 553
  - salivary glands, *i*, 593
  - scarlet, *i*, 548
  - scurvy, *i*, 550
  - smallpox, *i*, 548
  - stomatitis chr., *i*, 553
  - sublingual cysts, *i*, 507
  - sublingual glands, *i*, 507, 575
  - syphilis, *i*, 546, 553, 556, 575
  - teeth, *i*, 546, 576
  - tongue, *i*, 548, 554, 562
  - tonsils, *i*, 606
  - tuberculosis, *i*, 554
  - tumors, *i*, 564, 602
  - vesicular stomatitis, *i*, 548
  - Vincent's angina, *i*, 550
- Orchitis, *ii*, 1483, **1485**
  - epididymitis, *ii*, 1475, 1479, 1484, **1487**
  - leprosy, *ii*, 1493
  - paradidymitis, *ii*, 1461
  - and parotid gland, *i*, 594
  - periorchitis, *ii*, 1514
  - syphilis, *ii*, **1491, 1492**
  - tuberculosis, *ii*, 1415, **1487,** 1490
- Oriental boil, *i*, 212
- Ossification, *ii*, 1150, 1155, 1161
  - enchondral, *ii*, 1157, **1196**
  - endocard, *i*, 39
  - goiter, *i*, 521
  - larynx, *i*, 326
  - lymph nodes, *i*, 285
  - thyroid, *i*, 521
- Osteoarthritis, *ii*, 1235, 1239
- Osteoarthropathy, *ii*, 1082
- Osteoblasts, *i*, 286, *ii*, 1056
- Osteochondritis, *ii*, 1102, 1137, 1274
- Osteochondroma, *i*, **592,** *ii*, 1206
- Osteoclasts, *ii*, 1056
- Osteocytes, *ii*, 1056
- Osteofibroma, *ii*, **1194**
- Osteogenesis, *ii*, 1064, **1175, 1176, 1178**
- Osteoid-chondroma, *ii*, 1152
  - -sarcoma, *ii*, **1192, 1193, 1207**
  - -tissue, *ii*, 1152
- Osteolysis, *ii*, 1071
- Osteoma, *i*, 586, *ii*, 1195, 1199, *iii*, 2053, **2054**
  - of falx cerebri, *iii*, **1821**
  - of teeth, *i*, 586
- Osteomalacia, *ii*, 1054, 1062, 1064, **1073,** 1074
  - pelvic, *ii*, **1078**
  - puerperal, *ii*, **1076**
- Osteomyelitis, *i*, 190, *ii*, 1095, 1097, **1100,** 1101, 1103
- Osteophytes, *iii*, **1992**
- Osteoplastic carcinomas, *ii*, **1222, 1224**
- Osteoplasty, *i*, 286, *ii*, 1082
- Osteoporosis, *ii*, 1067, 1103
- Osteopsathyrosis, *ii*, 1063
- Osteosarcoma, *ii*, **1194, 1209, 1210**
- Osteosclerosis, *ii*, **1106**
  - and leukemia, *i*, 204
- Ostitis, *ii*, 1095, 1103, 1110, 1114
  - deformans (Paget's dis.), *ii*, 1107, **1108**
  - fibrous, *ii*, **1110, 1226**
  - ossifying, *ii*, 1106
  - tuberculous, *ii*, **1124, 1126, 1127, 1129, 1130, 1132**
- Otitis media, *i*, 614
  - and meninges, *iii*, **1826,** 1828
  - and nose, *i*, 295
- Ovary, *ii*, 1460, 1462, 1480, 1541 to 1549
  - abscess, *ii*, 1548
  - actinomycosis, *ii*, 1552
  - adhesions, *ii*, 1549
  - anatomy, *ii*, 1541
  - ascites, *ii*, 1566
  - bacteria, *ii*, 1594
  - calcification, *ii*, 1565
  - carcinoma, *ii*, **1564,** 1571, **1572, 1574, 1577**
  - castration, *iii*, 1702
  - corp. lut., *ii*, **1543,** 1618
  - corp. lut. of pregnancy, *ii*, 1542, 1618
  - cystadenoma, *ii*, **1556, 1558, 1559, 1560, 1566, 1578**
  - cystic degeneration, *ii*, 1551
  - cysts, *ii*, 1552, **1560, 1562, 1563,** 1596
  - degenerat., *ii*, 1551

Ovary, dermoid cysts, *ii*, 1568, 1580
  diverticuli, *ii*, 1592
  Douglas's cul de sac, *ii*, 1549, 1612
  echinococcus, *ii*, 1589
  epoophoron, *ii*, 1567
  follicles, *ii*, 1547, 1553
  folliculoma, *ii*, 1573
  gonorrhea, *ii*, 1549
  Graafian follicles, *ii*, 1542
  granulomas, *ii*, 1561
  granulosa cell tumors, *ii*, 1573
  hematomas, *ii*, 1548
  hemorrhage, *ii*, 1547
  hernia, *ii*, 1546
  hydrops, *ii*, 1553
  hyperemia, *ii*, 1544, 1547, 1551
  inflammation, *ii*, 1548
  lutein cells, *ii*, 1480
  lymphatics, *ii*, 1546
  menstruation, *ii*, 1544, 1618, 1619
  number at birth, *ii*, 1545
  ovarian cells, *ii*, 1568
  ovum, impregn., *ii*, 1618
  papilloma, *ii*, 1565, 1569
  parasites, *ii*, 1589
  paroophoron, *ii*, 1569
  parovarian cysts, *ii*, 1569, 1570
  pedicle, *ii*, 1565
  Pflüger's tubes, *ii*, 1566
  post mortem findings, *ii*, 1549
  pregnancy, *ii*, 1542, 1618
  primitive ovary, *ii*, **1461**
  psammocarcinoma, *ii*, 1564
  pseudomyxoma, *ii*, 1565
  puberty gland, *ii*, 1545
  removal, *iii*, 1702
  sarcoma, *ii*, 1578, **1579, 1581**
  senility, *ii*, 1546
  supernumerary ovaries, *ii*, 1546
  teratomas, *iii*, 1746
  torsion of pedicle, *ii*, 1565
  transplantation, *ii*, 1547
  tuberculosis, *ii*, 1551, 1565
  tubo-ovar. cysts, *ii*, 1554
  tumors, *ii*, 1555, 1557, **1575, 1576**
  tumors in children, *ii*, **1575,** 1576
Oxalate calculi, *ii*, 1412
Oxalic acid poisoning, *ii*, 1315
Oxidase reaction, *i*, 196
Oxyuris vermicularis, *ii*, 832, **833, 849,** 854
    in appendix, *ii*, 832
Ozena, *i*, 295

Pacchionian bodies, *iii*, 1805
Pachydermia, 2168
  laryngeal, *i*, **310**
  lymphangiectatic, *i*, 310
Paget's disease of bone, *ii*, 1107, **1108**
    of nipple, *iii*, 1787
Palate, *i*, 545, 557, 604
  abscess, *i*, 615, **616**
  carcinoma, *i*, **180, 182**
  cleft palate, *i*, 545
  diphtheria, *i*, **611**
  hyperemia, *i*, 605
Palate, inflammation, *i*, 606, 608
  malformation, *i*, 545
  palatoschisis, *i*, 545
  phlegmon, *i*, 615
  pseudomembranous infl., *i*, 608, **611**
  soft palate, *i*, 622
  syphilis, *i*, 553
  tuberculosis, *i*, **620**
  tumors, *i*, 622
  uvula, *i*, 605, 615
Paltauf's nannism, *ii*, 1180
Pancreas, *ii*, 1021
  aberrant, *ii*, 1021
  adenoma, *ii*, 1022
  amyloid degeneration, *ii*, 1038
  apoplexy, *ii*, 1024
  calculi, *i*, **596,** *ii*, 1030, 1043
  carcinoma, *ii*, 1046
  circulat., *ii*, 1022
  cirrhosis, *ii*, 1029
  cystadenoma, *ii*, **1044**
  cystoids, *ii*, 1049
  cysts, *ii*, 1021, 1027, **1048, 1049,** 1384
  degenerations, *ii*, 1033
  diabetes, *ii*, 1036
  ducts, *ii*, 1021
  enzymes, *ii*, 1026
  fat infiltration, *ii*, 1034
  fat necrosis, *ii*, 1022, 1038, **1039, 1041**
  hemorrhage, *ii*, 1022, **1023, 1024**
  induration, *ii*, 1029
  infection, *ii*, 1032
  inflammations, *ii*, 1025
  intestinal pancr., *i*, 728
  island theory, *ii*, 1036
  islands of Langerhans, *ii*, 1035
  lipomatosis, *ii*, 1038
  malformation, *ii*, 1021
  necrosis, *ii*, 1024, 1026
  pancreatitis, *ii*, 1025, **1030, 1031, 1032**
  parasites, *ii*, 1050
  pigmentation, *ii*, 1038
  pseudocysts, *ii*, 1027
  sarcoma, *ii*, 1045
  sclerosis, *ii*, **1029**
  syphilis, *ii*, 1032
  trauma, *ii*, 1042
  tuberculosis, *ii*, 1033
  tumors, *ii*, 1022, 1044
  Vater-Pacini-bodies, *ii*, 1050
Panophthalmia, *iii*, 1809
Papillary cyst adenoma, *i*, 521
Papilloma, bladder, *ii*, **1433, 1434**
  larynx, *i*, 310, 320, **321,** 324
  mouth, *i*, 565
  skin, *iii*, 2196
Papules, *iii*, 2074
Paraffinoma, *iii*, **2121**
Paraganglia, adrenal medulla, *ii*, 1276
  carotid gland, *i*, 330
  chromaffin cells, *ii*, 1277
  coccygeal gland, *i*, 331
  paraganglioma, *ii*, 1287, 1289
  Zuckerkandl's organ, *ii*, 1277

Paralysis agitans, *i*, 542, *iii*, 1913
  bulbar, progressive, *iii*, 1995
  intestinal, *i*, 744, 751
  Landry's progessive, *iii*, 1993
  myasthenic, *iii*, 1995
  neurogenous, *ii*, 1271
  Parkinson's, *i*, 507, 542, *iii*, 1913
  progressive, *iii*, 1866
  spastic spinal, *iii*, 1989, 1997
Paramastitis, *iii*, 1762
Parametritis, *iii*, 1644
Paranephritis, *ii*, 1420
Paraparesis, *iii*, 1997
Paraphimosis, *ii*, **1534,** 1535
Paraplegia, Brown-Sequard's, *iii*, 1985
Parasites and their locations, acarus, *iii*, 1803, 2155, **2156**
  ameba in mouth, *i*, 560
  ameba in pernic. anemia, *i*, 190, 208
  ameba-intestinal, *ii*, 847, **849,** 857
  anguillula, *ii*, 854
  ankylostoma, *ii*, **849, 853,** 854
  anopheles, *i*, 208, 209
  ascaris, *i*, 190, *ii*, 852, **849,** 1448
  balantidium, *ii*, 857
  bedbugs, *iii*, 2155
  bilharzia, *i*, 190, 211, *ii*, 856, 1447
  in blood, *i*, 190, 208, 212, 213, 214, 262, 305, 781
  in bone, *ii*, 1227
  bothriocephalus, *i*, 190, *ii*, **849,** 850
  in brain, *iii*, 1852, **1939**
  breast, *iii*, 1803
  cercomonas, *ii*, **849,** 857
  cestodes, *ii*, 847
  Chaga's disease, *i*, 212
  chrysops, *i*, 262
  coccidium, *ii*, 883
  comedo, *iii*, 1803, 2156, 2217
  conorhinus, *i*, 212
  cysticercus, *i*, 285, 576, *ii*, 848, 1402, *iii*, 1845, 1852, 1939, **2060**
  demodex, *iii*, 1803, 2156, 2217
  dermacentor, *i*, 262
  dermatozoa, *iii*, 2155
  distomum, *i*, 211, *ii*, 856, 978, 1402, 1447
  echino coccus, *i*, 86, **247,** 254, 285, 481, 505, 537, 576, *ii*, 971, **972, 974, 975,** 1227, 1291, 1447, 1589, 1601, *iii*, 1852, **1939**
  elephantiasis, *i*, 210
  epizoa, *iii*, 2155
  esophagus, *i*, 657
  eustrongylus, *ii*, 1402
  Fallopian tubes, *ii*, 1589, 1601
  fever, recurrent, *i*, 214
  fever, yellow, *ii*, 1020
  filaria, *i*, 210, **211,** *ii*, 1402, 1447
  flagelates, *ii*, 857
  fleas, *i*, 262, 406, *iii*, 2155
  flies, *i*, 212, 262, *iii*, 2155
  fly larvae, *iii*, 2155
  fungus diseases, *iii*, **2118, 2119, 2120,** 2149, 2152
  in gallbladder, *ii*, 1008
Parasites and their locations, glossina palpalis, *i*, 212
  in heart, *i*, 18, 86
  hookworm, *ii*, 853
  infusoria, *ii*, 858
  intestines, *i*, 211, 657, 751, 760, 781, *ii*, **833,** 847, **849, 853,** 856
  itch, *iii*, 2155
  ixodes, *iii*, 2155
  kala azar, *i*, 212, 236
  kidney, *ii*, 1402
  larynx, *i*, 327
  Laveran's crescents, *i*, 208
  Leishmania, *i*, 212, 236, *iii*, 2157
  leptospira icteroides, *ii*, 1020
  lice, *i*, 213, 781, *iii*, 2090, 2155
  liver, *ii*, 921, 971, **972, 974, 975**
  lungs, *i*, 406, 480, 481
  lymph nodes, *i*, 285
  lymphatics, *i*, 184
  malaria, *i*, 208, **209,** 235, *iii*, 1912
  merozoids, *i*, 209, 239
  microgametes, *i*, 209
  mosquitoes, *i*, 208, 211, 214
  mouth, *i*, 560, 576
  myiasis, *i*, 305
  nematodes, *ii*, 852
  nose, *i*, 304
  O'Hara's disease, *i*, 262
  omentum, *ii*, 870, 883
  oocytes, *i*, 209
  oxyuris, *ii*, **833, 849,** 852, 854, 1448, 1601, *iii*, 1698
  pancreas, *ii*, 1050
  pentastomum, *i*, 248, *ii*, 978
  pericardium, *i*, 18
  peritoneum, *ii*, 870, 883
  pest, *i*, 406
  pharynx, *i*, 613, 627
  plague, *i*, 406
  pleura, *i*, 495
  protozoa, *ii*, 857, *iii*, 2157
  psorospermia, *ii*, 1010
  pulex, *i*, 406, *iii*, 2155
  rats, *i*, 252
  Rickettsia, *i*, 782
  round worms, *ii*, 852
  scabies, *iii*, 2155
  schistogeny, *i*, 209
  schistosomum, *i*, 237, *ii*, 857
  skin, *iii*, 2155
  sleeping sickness, *i*, 211
  spinal cord, *iii*, 1964, 1990, 2012
  spirillae, *i*, 211, 613
  spirochetae, Duttonii, *i*, **214**
    -icterohem., *ii*, 1020
    -pallida, *i*, 215
  spleen, *i*, 245, **247**
  sporoblasts, *i*, 209
  sporozoads, *ii*, 858
  sporozoids, *i*, 209
  stegomya, *ii*, 1020
  tape worms, *ii*, 847
  tenia, *ii*, 847, **849**
  testicles, *ii*, 1510

- Parasites and their locations, thread worm, *ii*, 852
  - thyroid, *i*, 537
  - tick, *i*, 212, 214, *iii* 1912
  - tick fever, *i*, 212
  - trematodes, *ii*, 856
  - trichina, *i*, 212, 286, *iii*, **2056, 2057, 2058, 2060**
  - trichocephalus, *ii*, **849,** 855
  - trichomona, *ii*, **849,** 1448, *iii*, 1698
  - trypanosoma, *i*, 211, **212,** 236
  - tsetse fly, *i*, 212
  - tularemia, *i*, 262
  - vagina, *iii*, 1698
  - veins, *i*, 170
  - Weil's disease, *i*, 214, 219, *ii*, 1019
  - yellow fever, *ii*, 1020
- Parathyroid glands, *i*, 507, 538, **540**
  - calcium metabolism, *i*, 539
  - myasthenia gravis, *i*, 542
  - Parkinson's paralysis agitans, *i*, 507, 542, *iii*, 1913
  - tetany, *i*, 539, **540**
  - tumors, *i*, 538
- Paratyphoid, *i*, 761
- Paronychia, *iii*, 2223
- Paroophoron, *ii*, 1569
  - chromaffin cells, *ii*, 1277
- Parotid gland, abscess, *i*, 593
  - actinomycosis, *i*, 596
  - adenoma, *i*, **597**
  - mixed tumors, *i*, 181, 593, **601, 602, 603**
  - orchitis, *i*, 594
  - Stenson's duct, *i*, 593
  - tuberculosis, *i*, 595
  - tumors, *i*, 181, 593, **597, 601, 602, 603**
- Parovarian cysts, *ii*, 1569, 1570
- Parrot disease (psittacosis), *i*, 406
- Parulis, *i*, 578
- Patella, *iii*, **2066**
- Pearl disease, *i*, 17
- Pediculi, *i*, 213, 781, *iii*, 2090, 2155
- Pellagra, *iii*, **2002**
- Pelvis, *i*, **730, 731, 733,** *ii*, **1078, 1162, 1173, 1204, 1278**
  - chondrodystrophy, *ii*, **1173,** 1175
  - cleft pelvis, *ii*, **1078,** 1222, 1224
  - enchondroma, *ii*, **1204**
  - fetal malformation, *ii*, 1428
  - Naegele's oblique pelvis, *ii*, 1078, 1188
  - osteomalacia, *ii*, **1278**
  - Otto-Chrobak's pelvis, *ii*, 1266, 1269
  - rachitis, *ii*, **1162,** 1163
  - rotation, *ii*, 1267
  - torsion, *ii*, 1267
- Pemphigus, *i*, 197, *iii*, 2087, 2088
  - eosinophilia, *i*, 197
  - pemph. neonat., *iii*, 2088
- Penis, *ii*, 1533
  - bacteria, *ii*, 1534
  - balanitis, *ii*, 1533
  - calculi (prepuc.), *ii*, 1477, 1540
  - carcinoma, *ii*, 1538, **1539**
  - cavernitis, *ii*, 1535
- Penis, chancre, (Ducrey's), *ii*, 1534, 1535, *iii*, 2113
  - condylomas, *ii*, **1537**
  - corpora. cavern., *ii*, 1535
  - cysts, *ii*, 1478
  - elephantiasis, *ii*, 1537
  - epispadia, *ii*, 1424, 1448, **1477**
  - fracture, *ii*, 1537
  - gangrene, *ii*, 1533
  - glands, *ii*, 1533
  - gonorrhea, *ii*, 1534
  - granuloma inguinale, *ii*, **1536**
  - hermaphrotism, *ii*, 1466, **1481, 1483**
  - herpes, *iii*, 2086
  - horns, *ii*, 1538
  - hypospadia, *ii*, **1477**
  - induration, *ii*, 1535
  - inflammation, *ii*, 1533
  - leukoplakia, *ii*, 1538
  - malformation, *ii*, 1533
  - paraphimosis, *ii*, **1534,** 1535
  - phimosis, *ii*, 1477, 1534
  - posthitis, *ii*, 1533
  - prepuce, *ii*, 1477, 1533, **1536, 1537,** 1540
  - pseudohermaphrotism, *iii*, **1781**
  - soft chancre, *ii*, 1534, 1535, *iii*, 2113
  - smegma bacilli, *ii*, 1534
  - syphilis, *ii*, 1536, 1537
  - tumors, *ii*, **1538, 1539**
  - Tyson's gland, *ii*, 1533
  - ulcerations, *ii*, 1534
  - urethra, *ii*, 1478
- Pentastomum, *i*, 248, *ii*, 978
- Perforating canals of Volkmann, *ii*, 1053
- Perforations, aneurysm, *i*, 145
  - bladder, *ii*, 1429
  - esophagus, *i*, 634, 656, 657
  - intestines, *i*, 753, 801, *ii*, 837
  - peritoneum, *ii*, 863
  - stomach, *i*, 664, 672, **681, 682, 683,** 685
  - urethra, *ii*, 1519
- Periarteritis, *i*, 148
- Pericarditis, **6**
  - actinomycosis, *i*, 17
  - adhesions, *i*, 17
  - anemia, *i*, 15
  - bacteria, *i*, 15
  - cells, *i*, 9
  - cicatrico-mediastinal, *i*, 12
  - fibrino-purulent, *i*, 15
  - fibrinous, *i*, 18
  - granul. tumors, *i*, 16
  - granulat. tissue, *i*, 9
  - hemorrhagic, *i*, 16
  - ichorous, *i*, 14
  - nephritic, *i*, 15
  - petrification, *i*, 13
  - productive, *i*, 8, 12, 14
  - suppurative, *i*, 14, 15
  - syphilitic, *i*, 17
  - traumatic, *i*, 5, 16
  - uremic, *i*, 15
  - zuckerguss, *i*, 11
- Pericardium, *i*, 1
  - air in, *i*, 5

Pericardium, anthracosis, *i*, 5
  carcinoma, *i*, **18**
  contents, *i*, 1
  corpora libra, *i*, 18
  fat, *i*, 19
  granulation tissue, *i*, 9
  hemopericardium, *i*, 3, 16
  hydropericardium, *i*, 2, 145
  malformation, *i*, 1
  milk spots, *i*, **13**
  parasites, *i*, 18
  pearl disease, *i*, 17
  pericarditis, *i*, 6
  petrification, *i*, 13
  pneumopericardium, *i*, 5
  pulsus paradoxus, *i*, 3
  rupture, *i*, 3, 4
  sarcoma, *i*, 18
  scars, *i*, 12
  syphilis, *i*, 17
  trauma, *i*, 5, 16
  tuberculosis, *i*, 4, 16
  tumors, *i*, 16, 17, **18**
  zuckerguss, *i*, 11
Perichondritis, *i*, 313, 319
Peridontal cysts, *i*, 588
Perineal hernia, *i*, 734
Perinephritis, *ii*, 1419, 1420
Periosteum, *ii*, 1057
  periostitis, *i*, 296, *ii*, 1092, 1097, **1100,** 1101, 1114
  sarcoma, *ii*, **1209**
Periproctitis, *ii*, 842
Perisplenitis, *i*, 245
Perithelioma, *i*, 178
Peritoneum, *ii*, 858, *iii*, 1755
  abscess, *ii*, 876
  actinomycosis, *ii*, 872
  adhesions, *ii*, 871
  anatomy, *ii*, 859
  ascaris, *ii*, 883
  ascites, *ii*, 859, 872
  bacteria, *ii*, 867
  bile peritonitis, *ii*, 864
  blood-absorption, *ii*, 861
  calcification, *ii*, 870
  carcinoma, *ii*, 877
  circulation, *ii*, 862, 880
  coccidium, *ii*, 883
  cysts, *ii*, 874
  echinococcus, *ii*, 883
  endothelioma, *ii*, **876**
  focal abscess, *ii*, 876
  foreign bodies, *ii*, 870, 882
  hemoperitonitis, *ii*, 860
  hydrops, *ii*, 860
  inflammation, *ii*, 862, 875
  leukemia, *ii*, 872
  lymphatics, *ii*, 881
  mesentery, *ii*, **879**
  myxosarcoma, *ii*, **873**
  omentitis, *ii*, 869, 875
  organisms, passage of, *ii*, 860
  parasites, *ii*, 870, 883
  perforations, *ii*, 863
Peritoneum, peritoneal cavity, *i*, 559, 560
  peritonitis, *i*, 751, 753, 759, *ii*, 862, 1430, *iii*, 1755
  retroperitoneal tumors, *ii*, 873
  sarcoma, *ii*, **873,** 877, **879**
  scars, *ii*, 882
  tuberculosis, *ii*, 861, 870
  tumors, *ii*, 861, 872
  typhoid, *ii*, 872
Perityphlitis, *i*, 746
Pernicious anemia, *i*, 189, 191, 192
  bone marrow, *i*, 191
  liver diet, *i*, 191
  stomach, *i*, 667, 668, 713
Pertussis, *i*, 309
Pes calcaneus, *ii*, **1270**
    equinus, *ii*, **1270**
    valgus, *ii*, **1270**
    varus, *ii*, **1270**
Pest, bubonic, *i*, 252, 406
  fleas, *i*, 406
  lymph nodes, *i*, 252
  pneumonic, *i*, 406
  rats, *i*, 252
  spleen, *i*, 232
Petrification, *i*, 39
Peyer's patches, *i*, 203, 718, **788, 789, 790,** 797
Pflueger's tubes, *ii*, 1566
Phagocytes, *i*, 194
  phagocytosis, *i*, 187, 219, 250, 286
Pharynx, abscess, *i*, 615
  actinomycosis, *i*, 621
  adenoids, *i*, 618
  aleukemic adenia, *i*, 624
  amygdalitis, *i*, 606
  angina (Ludwig), *i*, 614
  bacilli, *i*, 608
  carcinoma, *i*, **624,** 625, 634
  catarrh, *i*, 617
  circulation, *i*, 605
  corrosive poisons, *i*, 673
  cysts, *i*, 622
  decubital necrosis, *i*, 627, **628**
  diphtheria, *i*, 294, 312, 608
  diverticuli, *i*, 629
  glanders, *i*, 621
  granulomas, *i*, 619
  inflammation, *i*, 606, 617
  laryngeo-tracheo-bronchitis, *i*, 312
  leprosy, *i*, 319, 620
  leukemia, *i*, 625
  lupus, *i*, 620
  lymphogranulomatosis, *i*, 624
  mixed infection, *i*, 614
  otitis media, *i*, 614
  parasites, *i*, 627
  pharyngitis, *i*, 606
  phlegmons, *i*, 615
  plasmocytoma, *i*, 625
  poisons, *i*, 628
  polyps, *i*, 622
  pseudomembranes, *i*, 608, 610, 614
  retropharyngeal abscess, *i*, 616
  sarcoma, *i*, 623
  scars, *i*, 621

Heavy face type denotes an illustration.

Pharynx, scleroma, *i*, 621
  sporotrichosis, *i*, 621
  staining methods, *i*, 611
  stains due to poisons, *i*, 622
  syphilis, *i*, 620
  tonsilitis, *i*, 606, 616
  tuberculosis, *i*, 619
  tumors, *i*, 621
  typhoid, *i*, 621
  Vincent's angina (trench mouth), *i*, 550, 560, 613, 616
Phimosis, *ii*, 1477, 1534
Phlebarteriectasis, *i*, 150
Phlebectasias, *i*, 161, 162, 166
  phlebitis, *i*, 156
  syphilis, *i*, 160
  thromobophlebitis, *i*, 156
Phlebogenous angiomas, *i*, 150
Phleboliths, *i*, 155, 230
Phlebomalacia, *i*, 161
Phlebosclerosis, *i*, 157
Phlegmasia alba dolens, *i*, 158
Phlegmons, angina phlegmonous, *i*, 615
  esophageal, *i*, 637
  laryngeal, *i*, 313
  lymphatic, *i*, 174
  orbital, *i*, 296
  pharyngeal, *i*, 615
  of stomach, *i*, 669
  of tongue, *i*, 550
  tonsils, *i*, 616
Phokomelia, *ii*, 1169
Phosgene, (war gas), *i*, 376
Phosphatic calculi, *ii*, 1412
Phosphorus, necrosis bone, *ii*, 1086, 1106, 1120, **1121**
  poisoning, heart, *i*, 5
  kidney, *ii*, 1316, 1322
  liver, *ii*, 907, 912
  muscles, *iii*, 2034, 2037
  stomach, *i*, 713
  tubes (Fallopian), *ii*, 1591
Phthisis, *i*, 437
Physometra, *ii*, 1616
Pia, *iii*, 1804, **1838**, 1960
Pigeon breast, *ii*, 1163
Pigment, adrenals, *ii*, 1275, 1276
  bile, *i*, 192
  birthmarks, *iii*, **2181**
  blood, *i*, 206, 210
  bronzing, *ii*, 1276
  coal, *i*, 372, 471
  freckles, *iii*, 2159
  gerontoxon, *iii*, 2160
  icterus, *i*, 222
  intestines, *i*, 759, 804
  lentigenes, *iii*, 2159
  leucoderma, *iii*, 2164
  liver, *ii*, 926, 950
  lungs, *i*, 372, 471
  lymph nodes, *i*, 254
  melanin, *i*, 210
  nevi, *iii*, 2159, 2172
  pancreas, *ii*, 1038
  seminal vesicles, *ii*, 1517
Pigment, skin, *ii*, 1283, *iii*, 2159
  spleen, *i*, 222
  viteligo, *iii*, 2164
  xanthoma, *iii*, **2160**
  xeroderma, *iii*, 2163, 2216
Pineal gland, epiphysis cerebri, *iii*, 1956
    hypoplasia, *iii*, 1958
    precocity, *iii*, 1958
    tumor, *iii*, **1957**
Pituitary gland, adenoma, *iii*, **1948**, 1950
    acromegaly, *iii*, 1949, 1954
    anatomy, *iii*, 1945
    bacteria, *iii*, 1955
    cachexia, *iii*, 1956
    degeneration, *iii*, 1947, 1955
    diabetes insipidus, *iii*, 1949
    dwarfism (Paltauf's), *ii*, 1180
    giantism, *iii*, 1954
    hyperpituitarism, *iii*, 1950
    inflammation, *iii*, 1951
    obesity, *iii*, 1950
    pregnancy, *iii*, 1947
    sella tursica, *iii*, 1950
    splanchnomegaly, *iii*, 1951
    syphilis, *ii*, 1155
    tuberculosis, *iii*, 1955
    tumors, *ii*, 1180, *iii*, **1948**, 1952, **1953**
Pityriasis, *iii*, 2152
Placenta, *iii*, 1710, 1718, 1720, 1727, 1733
  abortion, *ii*, 1621, 1632, *iii*, 1637
  air embolism, *i*, 207
  amnion, *iii*, 1710, 1714
  attachment, *ii*, 1611
  chorion epithelioma, *iii*, 1717, 1722, 1727, **1740, 1741, 1742, 1743**
  circulation, *iii*, 1713
  cysts, *iii*, 1733
  embolism, *i*, 207, *iii*, 1728
  fetus, *iii*, 1720, 1732
  giant cells, *iii*, 1717
  gonorrhea, *iii*, 1718
  hydatidiform mole, *iii*, **1722, 1725**
  hyperplasia, *iii*, 1733
  infarcts, *iii*, 1728
  infections, *iii*, 1718, 1732
  loosening, *iii*, 1715
  placentitis, *iii*, 1733
  polyps, *iii*, 1737, **1739**
  previa, *iii*, 1715, 1730
  puerperal infection, *iii*, 1732
  serotina, *iii*, 1714, 1718
  size, *iii*, 1731
  syncytioma, *iii*, 1717, 1722
  syncytium, *iii*, 1712, 1724
  tuberculosis, *iii*, 1732
  tumors, *iii*, 1730, 1733
  umbilicus, *iii*, 1711
  weight, *iii*, 1731
Plague, bubonic, *i*, 252
  pulmonic, *i*, 406
Plasma cells, *i*, 55
Plasmacytomas, *i*, 272, 564, 625
Plasmodium malariae, *i*, 208, **209**, 235, *iii*, 1912
Plethora, *i*, 77

Pleura, *i*, 482
  actinomycosis, *i*, 190
  adhesions, *i*, 484
  aneurysms, *i*, 145
  carcinoma, *i*, 495
  emphysema, *i*, 485
  empyema, *i*, 487
  endothelioma, *i*, 493
  exudate, *i*, 487
  hemorrhage, *i*, 483
  hemothorax, *i*, 483
  hydrothorax, *i*, 375, 482
  lymphosarcoma, *i*, 494
  neuroma, *i*, 492
  parasites, *i*, 495
  pleuritis, *i*, 486, 487
  pneumothorax, *i*, 364, 483, 484, 485
  post mortem, *i*, 484
  sarcoma, *i*, 492
  syphilis, *i*, 492
  trauma, *i*, 483
  tuberculosis, *i*, 489
  tumors, *i*, 492
  wounds, *i*, 483
Pleuritis, *i*, 397, 486
  adhesive, *i*, 486
  chronic fibrous, *i*, 486
  consequences, *i*, 488
  contracting, *i*, 489
  dry, *i*, 486
  exudative, *i*, 487
  fibrinous, *i*, 486
  hemorrhagic, *i*, 487
  purulent, *i*, 487
  suppurative, *i*, 487
  tuberculous, *i*, 489
Pneumatocele, *i*, 597
Pneumatosis, *i*, 767
Pneumococci, *i*, 389, **391**
Pneumoconiosis, *i*, 418, 420
Pneumomycosis, *i*, 480
Pneumonatemia, *i*, 207
Pneumonia, *i*, 376, 391
  acute, *i*, 414
  aspiration, *i*, 417, *ii* , 1121
  bacteria, *i*, **394,** 406
  bronchopneumonia, *i*, **403**
  carnification, *i*, **399**
  caseous, *i*, 408, 437
  in children, *i*, 260
  croupous, *i*, 389, 417
  fibrinous, *i*, 388, **393**
  gangrene, *i*, **409**
  gray hepatization, *i*, **394**
  influenzal, *i*, 341
  interstitial, *i*, 414
  kidney, *ii*, 1316, 1338
  lobar, *i*, 388
  lobular, *i*, 398, **407**
  peribronchial, *i*, 347
  pest pneum., *i*, 406
  pleurogenic, *i*, 416
  septic, *i*, 400, 414
  tuberculous, *i*, 425, 428, 432, 438, 439
Pneumopericardium, *i*, 5
Pneumothorax, *i*, 364, 483
  pseudopneumothorax, *i*, 484
Poikilocytosis, *i*, 192
Poisoning, amanita phalloides, *ii*, 903, **913,** 1380
  anilin, *i*, 215
  arsenic, *i*, 673, *ii*, 1315
  bichloride of mercury, *i*, 675, *ii*, 1302, 1315, **1379**
  blood, *i*, 6, 62, 73, 186, 190, 215
  botulism, *i*, 762
  cantharides, *ii*, 1315
  carbolic acid, *i*, 675, *ii*, 1315
  carbon monoxide, *i*, 215
  cheese, *iii*, 2080
  chloroform, *ii*, 1302
  chrome salts, *ii*, 1315
  coal gas, *i*, 215
  copaiba balsam, *ii*, 1315
  copper, *i*, 676
  corrosives, *i*, 73, 673
  esophagus, *i*, 638
  fish, *iii*, 2080
  food, *i*, 762, *iii*, 2080
  gall-bladder, *ii*, 981, 1012, 1015
  heart, *i*, 5, 52, 53
  intestines, *i*, 761, 770, 777
  iodoform, *ii*, 1315
  kidney, *ii*, 1315, 1316, 1337, **1379,** 1381
  larynx, *i*, 308
  lead, *i*, 188, 551, *ii*, 1315
  liver, *ii*, 908, 931, 938
  lungs, *i*, 376, 406
  mercury, *i*, 551
  methemoglobin, *i*, 215
  mouth, *i*, 550, 628
  mushrooms, *ii*, 903, 910, 913, 1380
  mussels, *iii*, 2080
  naphthol, *ii*, 1315
  nitric acid, *i*, 675
  nitrobenzol, *i*, 215
  nose, *i*, 293
  oxalic acid, *i*, 676, *ii*, 1315, 1381
  pharynx, *i*, 611, 628
  phenol, *i*, 675, *ii*, 1315
  phenylhydrazin, *i*, 215
  phosgene, *i*, 376
  phosphorus, *i*, 550, 673, *ii*, 1315, 1382, *iii*, 2034, 2037
  post mortem findings, *i*, 674, 676
  potassium chloride, *i*, 215, 676
  potassium cyanide, *i*, 676
  ptomaines, *i*, 762, 770
  pyrogallic acid, *ii*, 1315
  salivary glands, *i*, 551, 559
  silver nitrate, *i*, 676
  stomach, *i*, 672, 713
  styrax, *ii*, 1315
  sublimate of mercury, *i*, 675, *ii*, 1302, 1315, **1379**
  sulphuric acid, *ii*, 1315
  terpentine, *ii*, 1315
  throat, *i*, 628
  toad stools, *ii*, 903, 913, 1380
  tongue, *i*, 628

Heavy face type denotes an illustration.

Poisoning, tubes, Fallopian, *ii*, 1591
  uranium, *ii*, 1337
  war gas, *i*, 376
Poliomyelitis, ac. ant., *iii*, 1990
Polychromatophilia, *i*, 192
Polycythemia, *i*, 187
Polymastia, *iii*, 1759
Polymyositis, *iii*, 2040
Polyps, bladder, *ii*, **1433, 1434**
  false vocal chords, *i*, **320**
  intestinal, *i*, 746, 760, 775, **810, 811, 812**
  larynx, *i*, 316, **320**
  nose, *i*, 296, 301, **302**
  pharynx, *i*, 622
  placenta, *iii*, 1737, **1739**
  trachea, *i*, 337
  uterus, *ii*, 1625, 1632, *iii*, **1633, 1654,** 1669, 1672
Polyuria, *ii*, 1529
Portal vein, *i*, 100, 158, *ii*, 894
  caput medusae, *i*, 105
  congestion, *i*, 223
  thrombophlebitis, *ii*, 893
  thrombosis, *i*, 223
Postmortem findings, air embolism, *i*, 207
  anemia-pernicious, *i*, 191
  blood, *i*, 189
  chloroma, *i*, 274
  epicardium, *i*, 72, 81
  esophagus, *i*, 632
  heart, *i*, 2, 38, 72, 81
  kidney, *ii*, 1298, 1352
  liver, *ii*, 887
  lungs, *i*, 358
  lymph, *i*, 216
  meninges, *iii*, 1810
  ovary, *ii*, 1549
  pericardium, *i*, 2
  pleura, *i*, 484
  post mortem tubercle, *iii*, 2127
  stomach, *i*, 658, 675, 714
  thoracic duct, *i*, 173
  uterus-puerperal, *iii*, 1748
Pott's disease, *ii*, **1129, 1130, 1132,** 1267
Pregnancy, *ii*, 1603, 1604, 1609, *iii*, 1708, 1716
  abdominal pregn., *ii*, 1603, 1610
  abdominal pressure, *ii*, 1614
  abortion, *ii*, 1621, 1632, *iii*, 1737
  abortion, incomplete, *ii*, 1621
  adhesions, *ii*, 1611
  amnion, *iii*, 1710, 1711, 1714
  amniotic fluid, *ii*, 1270, *iii*, 1719, 1720
  bacteria, *iii*, 1722, 1732
  blood mole, *iii*, 1735, 1736
  childbirth, *ii*, 1614
  chloasma, *iii*, 2162
  chorion, *iii*, 1710, 1716
  chorion epithelioma, *iii*, 1717, 1722, 1727, **1740, 1741, 1742, 1743**
  corpus luteum, *ii*, 1618
  cotyledons, *iii*, 1714, 1722
  deciduae, *iii*, 1708, 1717, 1739, 1751
  dysmenorrhea, *iii*, 1737
  eclampsia, *iii*, 1717

Pregnancy, edema, *iii*, 1701
  endometritis, *iii*, 1718
  extrauterine preg., *ii*, 1603, 1604, 1609, **1610**, *iii*, 1737
  fetus, *iii*, 1732
  fetus malformation, *iii*, 1720
  gonorrhea, *iii*, 1718
  hydatiform mole, *iii*, **1722,** 1724, **1725,** 1727, 1739, 1742, 1745
  hydramnion, *iii*, 1720
  hydrorrhea, *iii*, 1720
  intrauterine fetal death, *iii*, 1735
  involution, *iii*, 1718
  kidney, *iii*, 1727
  Langhan's cells, *iii*, 1712, 1745
  liver, *ii*, **897**
  lochia, *iii*, 1717
  membranes, fetal, *iii*, 1710, 1718
  oligohydramnion, *ii*, 1270
  ovum, *iii*, 1708, 1711
  placenta, *iii*, 1710, 1718, **1720,** 1731, 1733
  placenta previa, *iii*, 1715, 1730
  placental cysts, *iii*, 1733
  placental infarcts, *iii*, 1728
  placental polyps, *iii*, 1737, **1739**
  placentitis, *iii*, 1733
  serotina, *iii*, 1714, 1718
  syncytiolysins, *iii*, 1717
  syncytioma, *iii*, 1717, 1722
  syncytium, *iii*, 1712, 1724
  syphilis, *iii*, 1734
  thrombi, *iii*, **1728**
  tuberculosis, *iii*, 1732
  umbilicus, *iii*, 1711, 1733, 1735
  uterus, *iii*, 1708, 1717
Prepuce, *ii*, 1477, 1533, 1535
  calculi, *ii*, 1477, 1540
  condylomas, *ii*, **1537**
  elephantiasis, *ii*, 1537
  glands, *ii*, 1533
  herpes, *iii*, 2086
  smegma, *ii*, 1534
  syphilis, *ii*, 1536, **1537,** *iii*, **2130**
Prickly heat, *iii*, 2085
Proctitis, *ii*, 842, **843**
  syphilitic, *ii*, **843**
Progressive paralysis, *iii*, 1993
Prolapsus, rectum, *i*, 741, **743,** 744
  tongue, 572
  vagina, *ii*, 1612, **1613,** *iii*, 1699
  uterus, *ii*, 1612, **1613**
Prosopochisis, *i*, 546
Prostate, *ii*, 1448, 1453, 1517
  abscess, *ii*, 1518
  actinomycosis, *ii*, 1532
  anatomy, *ii*, 1517
  calculi, *ii*, 1520
  carcinoma, *i*, 175, *ii*, 1528, **1529, 1530, 1531**
  corpora amylacea, *ii*, 1520
  echinococcus, *ii*, 1533
  degeneration, *ii*, 1521
  gonorrhea, *ii*, 1519
  hematuria, *ii*, 1528
  Home's lobe, *ii*, **1522**
  hypertrophy, *ii*, **1522, 1523, 1524, 1527**

Heavy face type denotes an illustration.

Prostate, malformation, *ii*, 1521
  parasites, *ii*, 1533
  periprostatitis, *ii*, 1519
  prostatitis, *ii*, 1518
  prostatorrhea, *ii*, 1518
  rhabdomyoma, *ii*, **1532**
  sarcoma, *ii*, 1532
  senile atrophy, *ii*, 1522
  syphilis, *ii*, 1520
  tuberculosis, *ii*, 1519
  tumors, *i*, 175, *ii*, 1528
Protagon, *ii*, 1319
Protozoa, *ii*, 857
Prowazeki bodies, *i*, 782
Prurigo, *iii*, 2098
Pruritus vaginae, *ii*, 1702
Psammoma, dura, *iii*, **1816**
  psammous fibroendothelioma, *iii*, **1817, 1818**
  psammosarcoma, *iii*, **1820, 1821**
Pseudoaneurysm, *i*, 132
Pseudoarthrosis, *ii*, 1089, 1191
Pseudocysts, *ii*, 1027
Pseudohermaphrotism, *ii*, 1291, **1481**
Pseudoleukemic anemia of infants, *i*, 193
  pseudoleukemia, *i*, 205, 265, 339
Pseudomembranes, *i*, 610
  esophagus, *i*, 636
  intestines, *i*, 768
  larynx, *i*, **311**
  mouth, *i*, 549, 608, 614
  nose, *i*, 294
  pharynx, *i*, 608, 610, 614
  stomach, *i*, 669
  trachea, *i*, **332**
Pseudomyxoma, *ii*, 1565
Psittacosis, *i*, 406
Psoas abscess, *ii*, 1128
Psoriasis, *iii*, 2097
Psorospermia, *ii*, 1010
  Darier's disease, *iii*, 2157
Ptomains, *i*, 762, 770
Ptosis, kidney, *ii*, 1299
  liver, *ii*, 890
  stomach, *i*, 716
Ptyalism, *i*, 551
Puerperium, *ii*, 1624
  bacteria, *iii*, 1749, 1755
  endometritis, *iii*, 1751
  gas gangrene, *iii*, 1755
  infection, *iii*, 1749, 1750, 1755
  lochia, *iii*, 1717
  metrolymphangitis, *iii*, 1753
  metrophlebitis, *iii*, 1752
  nephritis, *iii*, 1727
  neuritis, *iii*, 2018
  osteomalacea, *ii*, **1076**, 1164, 1177
  peritonitis, *iii*, 1755
  phlegmasia alba dolens, *i*, 158
  phlegmonous metritis, *iii*, 1754
  puerperal fever, *iii*, 1754
  streptococci, *iii*, 1750
  trauma, *iii*, 1748, 1754
  tuberculosis, *iii*, 1751
Pulex-flea, *i*, 406, *iii*, 2155
Pulp granuloma, *i*, 586
    pulpitis, *i*, 577
Pulsion diverticuli, *i*, 653
Pulsus paradoxus, *i*, 3
    hard pulse, *i*, 110
    pulse, *i*, 110
Puncture, lumbar, *iii*, 1830
Pupil, *iii*, 2033
Purpura hemorrhagica, *iii*, 2071, 2072
  purpura neonatorum, *i*, 509
Pustule, *i*, 213
  anthrax, *iii*, 2107
Pyelitis, *ii*, 1417, 1429
Pyelonephritis, *ii*, 1362, **1363**, 1528
Pyemia lymphatic, *i*, 174
Pylorus, *i*, 660, 698, **701, 702**, 714
  pylorospasm, *i*, 660
  sarcoma, *i*, 692, **693**
  stenosis congenital, *i*, 660, 713
Pyometra, *ii*, 1616
Pyorrhea, *i*, 578
Pyosalpinx, *ii*, 1595

RABIES, *iii*, 1900
  Negri bodies, *iii*, 1900
Rachischisis, *ii*, 1165, *iii*, 1971
Rachitis, *ii*, 1151 to 1166
  craniotabes, *ii*, 1165
  dwarfism, *ii*, 1163
  femur, *ii*, **1153**
  fontanelles, *ii*, 1164
  funnel-breast, *ii*, 1163
  hydrocephalus, *ii*, 1164
  pelvis, *ii*, **1162**
  pigeon breast, *ii*, 1163
  rachitis tarda, *ii*, 1163
  rosary, *ii*, 1163
  skull, *ii*, 1164
  vertebrae, *ii*, 1163
Rag-picker's disease, pulmon. anthrax, *i*, 405
Ranula, *i*, 507, 574
Rats, *i*, 252
Raynaud's symmetric gangrene, *iii*, 2110, 2147
v. Recklinghausen's neurofibromatosis of skin, *iii*, **2027**
Rectocele, *ii*, 1612
Rectum, *i*, 722
  actinomycosis, *i*, 803
  atresias, *i*, 723
  carcinoma, *i*, 806, **814**, *iii*, 1697
  dysentery, *i*, **765**
  fissures, *ii*, 841
  fistulas, *i*, 740, *ii*, 842
  gonorrhea, *ii*, 845, *iii*, 1693
  hemorrhoids, *i*, 754, *ii*, 841
  invagination, *i*, 741, 745
  papillary adenofibroma, *i*, **809**
  periproctitis, *ii*, 842
  proctitis, *ii*, 842, **843**
  prolapsus, *i*, 741, **743**, 744
  sarcoma, *ii*, **826**
  syphilis, *ii*, 842, **843**
  trauma, *ii*, 845
  tuberculosis, *i*, 796

Heavy face type denotes an illustration.

- Rectum, tumors, *i*, 806, **809**, **814**, *ii*, **826**
- Relapsing fever, *i*, 783
- Renal pelvis, *ii*, 1311, 1375, **1403**, **1406**
  - concretions, *ii*, 1377
  - tuberculosis, *ii*, 1308, 1322, 1365, **1366**, **1369**, **1371**
- Respiratory organs, *i*, 292
  - bronchi, *i*, 337
  - larynx, *i*, 305
  - lungs, *i*, 358
  - nose, *i*, 292
  - pleura, *i*, 482
  - trachea, *i*, 327
- Reticulo-endothelial apparatus, *i*, 250, 286
- Retina, embolism retinal artery, *i*, **119**
  - glioma, *iii*, 1920
  - retinitis, *i*, 119
  - tumors, *iii*, 1920
- Retroflexion uteri, *ii*, 1611
- Retroperitoneal tumors, *ii*, 873
- Retropharyngeal abscess, *i*, 616
- Rhabdomyoma, bladder, *ii*, **1437**
  - heart, *i*, **84**, *iii*, 2055
  - kidney, *ii*, **1394**
  - mouth, *i*, 572
  - prostate, *ii*, **1532**
  - testicle, *ii*, **1495**
  - vagina, *iii*, 1696
- Rhagades, *i*, 311, 553
- Rheumatism, *ii*, 1236
  - heart, *i*, **27**, 28, 63
  - pericarditis, *i*, 15
- Rhinitis, *i*, 294
- Rhinoliths, *i*, 304
- Rhinophyma, *iii*, 2105
- Rhinoscleroma, *i*, 300
- Rice bodies of joints, *ii*, 1257, 1275
- Rickets, *ii*, 1151, 1163
- Rickettsia-Prowazeki, *i*, 782
- Rigor mortis, *iii*, 2033
- Rosary, rachitic, *ii*, 1163
- Rose spots of typhoid, *i*, 121, 781
- Round worms, *ii*, 852
- Rupture, aneurysms, *i*, 139
  - bladder, *ii*, 1446
  - ectopic gestation, *ii*, 1606, 1608
  - esophagus, *i*, 647, 656
  - heart, *i*, 4, 54, 69
  - hernias, *i*, 728
  - lymphatics, *i*, 176
  - pericardium, *i*, 4
  - spleen, *i*, 232
  - vein, *i*, 162
  - uterus, *ii*, 1616
- Russell bodies, *i*, 300

- SACRAL tumors, *iii*, 1976
- Salivary glands, *i*, 593
  - actinomycosis, *i*, 596
  - adenoma, *i*, **598**
  - angina, Ludwig's, *i*, 595
  - calculi, *i*, 596
  - carcinoma, *i*, 597
  - cyanche, *i*, 595
  - fistulas, *i*, 596

- Salivary gland, granulomas, *i*, 595
  - Ludwig's angina, *i*, 595
  - mixed tumors, *i*, 595, 598, 600, 601, 602, 603
  - parotid gl., *i*, 593, 602
  - parotitis, *i*, 594
  - pneumatocele, *i*, 597
  - poisoning, *i*, 551, 595
  - sarcoma, *i*, 599
  - silialocele, *i*, 596
  - testicles, *i*, 594
  - tumors, *i*, 181, 597, **598**, 600, **601**, **602**, **603**
- Salpingitis, *ii*, 1592, 1593
- Sarcoids, *iii*, 2129
- Sarcoma, adrenals, *ii*, 1291
  - in arteries, *i*, 152
  - bladder, *ii*, **1438**
  - of bone, *ii*, **1053**, **1191**, **1192**, **1193**, **1194**, **1207**, **1208**, **1209**, **1210**, **1211**, **1212**, **1213**, **1214**, **1225**
  - breast, *iii*, **1781**, **1785**, **1786**
  - diaphragm, *iii*, **1665**
  - dura, *iii*, **1822**
  - epuli, *ii*, 1215
  - esophagus, *i*, 639
  - fibrosarcoma, *iii*, **2190**
  - foot, *iii*, **2193**
  - gall bladder, *ii*, 1002
  - gums, *i*, 573, *ii*, 1215
  - heart, *i*, 18, 60, 67, 85, *iii*, **1665**
  - intestines, *ii*, 824, **825**, **826**, **827**
  - kidney, *ii*, **1392**, **1394**
  - larynx, *i*, 323
  - liver, *i*, 257, *ii*, 957
  - lungs, *i*, 475, **479**
  - lymph nodes, *ii*, **275**, 279, 281, 282
  - lymphatics, *i*, 179, 182
  - mediastinum, *i*, 503
  - melanosarcoma, *ii*, **958**, *iii*, **2193**, **2194**
  - meninges, *iii*, **1966**
  - mesentery, *ii*, **879**
  - metastases, *i*, 167
  - mouth, *i*, 573
  - myxosarcoma, *iii*, **2191**
  - nose, *i*, 293
  - ovary, *ii*, 1578, **1579**, **1581**
  - pancreas, *ii*, 1045
  - pericardium, *i*, 17
  - periosteum, *ii*, **1209**
  - peritoneum, *ii*, **873**, 877
  - pharynx, *i*, 623
  - pia, *iii*, **1838**
  - pleura, *i*, 492, 781
  - salivary glands, *i*, 599
  - sarcoma phyllodes, *iii*, **1781**
  - spleen, *i*, 246, *iii*, **1665**
  - stomach, *i*, 692, **693**
  - testicles, *ii*, 1496
  - thyroid, *i*, 534
  - tongue, *i*, 572
  - uterus, *iii*, **1664**, **1668**
  - vessels, *i*, 167
- Scabies, *iii*, 2155
- Scalp, carcinoma, *iii*, **2220**
  - granulomas, *iii*, **2116**, **2118**, **2119**, **2120**

Heavy face type denotes an illustration.

Scarlet fever, *iii*, 2076
    and diphtheria, *i*, 614
    kidney, *i*, 614, *ii*, **1329**, 1338, 1340, 1374
    lymph nodes, *i*, 614
    otitis media, *i*, 614
    scarlet fever-line, *iii*, 2076
    streptococci, *i*, 614
    tongue, *i*, 548
Scars, heart, *i*, 12, 13, **60**, **64**, **67**, 68
  kidney, *ii*, 1308
  peritoneum, *ii*, 882
  pharynx, *i*, 621
  spleen, *i*, 228
  stomach, *i*, 670, 685
Schistogeny, *i*, 209
Schistosoma, hematobium, *i*, 237
  japonicum, *ii*, 857
Scleroderma, *iii*, 2170
Scleroma, larynx, *i*, 320
  pharynx, *i*, 621
Sclerosis, arteries, *i*, 101, 103, 108, 109
  bone, *ii*, 1143
  heart, *i*, 23
  pancreas, *ii*, **1029**
  vessels, *i*, 108
Scoliosis, *ii*, 1066, 1079, 1163
Scrofuloderma, *iii*, 2101
Scrotum, *ii*, 1476
  carcinoma, *ii*, 1540
  edema, *ii*, 1533
  elephantiasis, *ii*, 1537
  gangrene, *ii*, 1533
  hydrocele, *ii*, 1484, 1511, **1512**
  syphilis, *ii*, 1537
  tumors, *ii*, 1537, 1540
Scurvy, *i*, 550, *iii*, 2073
  Barlow's infantile scurvy, *ii*, 1166, *iii*, 2074
Seborrhea, *iii*, 2216
Semen, *ii*, 1510
  Florence's reaction of semen, *ii*, 1518
  spermatogenesis, *ii*, 1480, 1482, 1511
Seminal vesicles, *ii*, 1515
Sequestrae, *ii*, 1117, **1118**, 1121, 1126
Sex-organs, *ii*, **1458**, 1464, **1465**
  and adrenals, *ii*, 1279
  asexuality, *ii*, 1466
  bladder, *ii*, **1458**
  castration, *ii*, 1186, *iii*, 1702
  descent of testicle, *ii*, 1462
  development, *ii*, 1458
  ectopic gest., *ii*, 1466, 1478
  epididymis, *ii*, 1479
  female, *ii*, 1461
  Gartner's duct, *ii*, 1459, 1464
  genital cells, *ii*, 1460, *iii*, 1680
  genital furrow, *i*, 723
  genital ridges, *ii*, 1460
  Giraldo's organ, *ii*, 1461
  gubernaculum testes, *ii*, 1460, 1476
  hermaphrotism, *ii*, 1466, 1467, **1481**, **1483**
  homosexuality, *ii*, 1482
  hypergenitalism, *ii*, 1174
  hypogenitalism, *ii*, 1180
  kidney, primitive, *ii*, **1458**
  male, *ii*, 1450
Sex-organs, malformation, *ii*, 1466, 1475
  menstruation, *ii*, 1618
  mesonephron, *ii*, **1458**
  Mueller's duct, *ii*, **1458**, 1460, 1464
  ovary, *ii*, 1545
  penis, *ii*, 1476, 1533
  precocity, *iii*, 1958
  prepuce, *ii*, 1477
  prostate, *ii*, 1477, 1517
  puberty glands, *ii*, 1460, 1461, 1480, 1482, 1545
  rejuvenation, *ii*, 1482
  semen, *ii*, 1510
  seminal vesicles, *ii*, 1515
  senility, *ii*, 1510, 1522
  Sertoli's cells, *ii*, 1480
  spermatic cord, *ii*, 1476
  spermatozoa, *ii*, 1510
  Steinach's experiments, *ii*, 1481
  testicle, *ii*, 1460, 1478
  trigone, *ii*, 1459
  tumors, *ii*, 1464, 1587
  ureters, *ii*, 1459
  uterus, *ii*, 1464, 1611
  vagina, *ii*, 1464, *iii*, 1693
  vulva, *iii*, 1700
  Wolffian body, *ii*, **1458**
Sharpey's fibres, *ii*, 1056
Siderosis, *i*, 422
Sigmoid, *i*, 718, 746
  carcinoma, *i*, **696**, **815**, *ii*, **819**, **820**
  dilatation, *i*, **752**
  hernia, *i*, 738
  Hirschsprung's disease, *i*, 721
  lipoma, *i*, **808**
  polyps, *i*, **810**
Silialocele, *i*, 596
Sinus, ethmoidal, *i*, 296
  frontal, *i*, 296
  maxillary, *i*, 296
  of Valsalva, *i*, 33, 124
Skeleton, of cretin, *ii*, **1185**
  defective, *ii*, 1161, 1169
  hypoplasia, *ii*, 1179
Skin, *iii*, 2036
  acanthosis nigricans, *iii*, 2168
  acarus scabeii, *iii*, 2155, **2156**
  achorion, *iii*, **2149**
  acne, *iii*, 2104, 2106, 2220
  acrocyanosis, *iii*, 2111
  actinomycosis, *iii*, 2147
  Addison's disease, *ii*, 1279, 1283
  adenoma, *iii*, 2196
  adiposis dolorosa, *iii*, 2175
  adrenals, *ii*, 1279, 1283
  ainhum, *iii*, 2111
  albinos, *iii*, 2164
  Aleppo boll, *iii*, 2158
  amyloid changes, *iii*, 2215
  anasarca, *iii*, 2065
  anemia, *iii*, 2069
  angioma, *iii*, **2181**
  anthrax, *iii*, 2107
  argyria, *ii*, 1381
  arsenic, *iii*, 2166

Heavy face type denotes an illustration.

- Skin, asteatosis, *iii*, 2216
  - atheroma, *iii*, 2217
  - atrophy, *iii*, 2213
  - bacteria, *iii*, 2070, 2072, 2077, 2102, 2109, 2113, 2145
  - bed bugs, *iii*, 2155
  - bed sores, *iii*, 2108
  - birth marks, *iii*, 2159
  - blastomycosis, *iii*, 2154
  - blisters, *iii*, 2074, 2081
  - boils, *iii*, 2158
  - Bright's disease, *iii*, 2072
  - bronzing, *ii*, 1283
  - bubo, *iii*, 2114
  - burns, *iii*, 2081, 2082
  - carbuncle, *iii*, 2106
  - carcinoma, *iii*, **2101, 2102, 2103, 2104, 2105, 2106, 2107, 2112,** 2199, **2220**
  - chancre, soft, *iii*, 2113
  - chloasma, *iii*, 2162
  - chondroma, *iii*, 2180
  - circulation, *iii*, 2069
  - clavus, *iii*, 2166
  - coccidia, *iii*, **2155**
  - comedos, *iii*, 1803, 2155, 2217
  - condylomas, *iii*, 2136
  - corion, *iii*, 2071, 2187
  - cornification, *iii*, 2172
  - corns, *iii*, **2166**
  - cow itch, *iii*, 2080
  - cowpox, *iii*, 2096
  - crusts, *iii*, 2074
  - cysts, *iii*, 2178, 2218
  - Darier's dis., *iii*, 2157
  - decomposition, *iii*, 2068
  - decubitus, *iii*, 2108
  - demarkation, *iii*, 2084
  - demodex, *iii*, 1803, 2155, 2217
  - dermatitis, *iii*, 2074
  - dermatomycosis, *iii*, 2148
  - dermatozoa, *iii*, 2155
  - dermoids, *iii*, **2218**
  - desquamation, *iii*, 2075
  - diabetes, *iii*, 2161
  - dourine, *iii*, 2158
  - drug exanthema, *iii*, 2081
  - ecthyma, *iii*, 2091
  - eczema, *iii*, 2089
  - edema, *iii*, 2069
  - electric burn, *iii*, 2081
  - elephantiasis, *iii*, **2112, 2169**
  - emphysema, *i*, 485
  - endothelioma, *iii*, 2198
  - ephelides, *iii*, 2159
  - epithelioma, *iii*, 2196, **2198**
  - epithelioma molluscum, *iii*, 2155, 2168
  - epizoa, *iii*, 2155
  - ergotism, *iii*, 2109
  - erysipelas, *iii*, 2101
  - erythema, *iii*, 2078
  - erythema nodosum, *iii*, 2079
  - erythrasma, *iii*, 2155
  - erythroderma, *iii*, 2069
  - exanthemata, *iii*, 2075, 2151
  - favus, *iii*, **2149**
- Skin, fibromas, *iii*, **2173**
  - Finsen light, *iii*, 2084
  - fleas, *iii*, 2155
  - flies, *iii*, 2155
  - food-poisons, *iii*, 2080
  - Fraenkel's gas bacillus, *iii*, 2070
  - framboesia, *iii*, 2138
  - freckles, *iii*, 2159
  - frost-bite, *iii*, 2081, 2084, **2085**
  - fungus diseases, *iii*, 2148
  - furuncle, *iii*, 2105, 2220
  - gangrene, *iii*, 2084, **2085, 2108,** 2111
  - gerontoxon, *iii*, 2160
  - glanders, *iii*, 2147
  - granuloma, *iii*, 2114, **2116, 2118, 2119, 2120**
  - gummas, *iii*, 2138, **2139, 2140**
  - hair, *iii*, 2090
  - heel-ulcer, *iii*, 2109
  - hemangioma, *iii*, 2181, **2182, 2183,** 2184
  - hematidrosis, *iii*, 2071
  - hemorrhage, *iii*, 2071
  - herpes, *iii*, 2078
  - herpes tonsurans, *iii*, 2150
  - herpes zoster, *iii*, 2186
  - hidradenoma, *iii*, 2199, **2200**
  - horns, *iii*, 2166, 2200
  - hospital gangrene, *iii*, 2109
  - hydrops, *iii*, 2071
  - hyperemia, *iii*, 2069
  - hyperidrosis, *iii*, 2221
  - hypertrophy, *iii*, 2166
  - hypomycetes, *iii*, 2153
  - ichthyosis, *iii*, **2171**
  - impetigo contag., *iii*, 2091
  - infiltration anesthesia, *iii*, 2070
  - inflammation, *iii*, 2074
  - insect bites, *iii*, 1912, 2070, 2073, 2080, 2090, 2155
  - intertrigo, *iii*, 2090
  - itch, *iii*, 2155
  - kala azar, *iii*, 2158
  - keloid, *iii*, **2174, 2175**
  - keratoma, heredit., *iii*, 2172
  - keratosis, *iii*, 2211
  - Koplik's spots, *iii*, 2076
  - leg-ulcers, *iii*, 2112, **2136,** 2158
  - Leishman-Donovan bodies, *iii*, 2158
  - lentigenes, *iii*, 2159
  - leprosy, *iii*, 2142, **2146**
  - leukoderma, *iii*, 2164
  - leukopathia, *iii*, 2164
  - lice, *iii*, 2090, 2155
  - lichen, *iii*, 2100
  - lightning stroke, *iii*, **2083**
  - lipoma sarcomatodes, *iii*, **2178**
  - lipomas, *iii*, **2177, 2178**
  - livor, *iii*, 2068
  - lupus, *iii*, 2099, **2122, 2123**
  - lymphangioma, *iii*, **2185, 2186, 2187**
  - macula, *iii*, 2074
  - malignant edema, *iii*, 2070
  - measles, *iii*, 2075
  - melanin, *iii*, 2185
  - melanosarcoma, *iii*, **2193, 2194**
  - melanosis, *iii*, 2163, 2192

Heavy face type denotes an illustration.

Skin, microsporia, *iii*, **2152**
  miliaria, *iii*, 2085
  milium, *iii*, 2217
  Moeller Barlow's dis., *iii*, 2074
  molluscum contag., *iii*, 2152, 2156
  mongolianism, *iii*, 2159
  morbilli, *iii*, 2075
  Morvan's disease, *iii*, 2147
  mumification, *iii*, 2108
  mycosis, *iii*, 2153
  myiasis, *i*, 305
  myoma, *iii*, 2176
  myxedema, *iii*, 2070
  myxoma, *iii*, 2180
  myxosarcoma, *iii*, 2191
  nails, *iii*, 2223
  necrosis, *iii*, **2085, 2108,** 2110
  negro, *iii*, 2164
  neurofibroma, *iii*, 2144
  neuroses, *iii*, 2099
  nevi, *iii*, 2159, 2172, **2173, 2181, 2187, 2189**
  nodules, *iii*, 2074
  oriental boil, *iii*, 2150
  pachidermia, *iii*, 2168
  Paget's disease, *iii*, 2111
  papilloma, *iii*, 2196
  papules, *iii*, 2074
  paraffinoma, *iii*, **2121**
  parasites, *iii*, 2090, 2155
  pemphigus, *iii*, 2087
  perforating ulcer, *iii*, 2109
  pigmentation, *ii*, 1278, 1283, *iii*, 2158, 2189, 2190
  phlegmon, *iii*, 2103
  pityriasis, *iii*, **2152**
  plica polonica, *iii*, 2090
  poisons, *iii*, 2070, 2074, 2078, 2080
  post mortem changes, *iii*, 2068
  prepuce, *iii*, **2130**
  protozoa, *iii*, 2157
  prurigo, *iii*, 2098
  psammoma, *iii*, 2199
  psoriasis, *iii*, 2097
  psorospermiosis, *iii*, 2157
  purpura hemorrh., *iii*, 2071, 2073
  purpura rheum., *iii*, 2079
  pustule malign, *iii*, 2107
  pustules, *iii*, 2074
  radium-burn, *iii*, 2114
  Raynaud's disease, *iii*, 2110, 2147
  rhagades, *iii*, 2074
  rhinophyma, *iii*, 2105
  rhinoscleroma, *iii*, 2147
  sarcoma, *iii*, **2160, 2178, 2190, 2191,** 2192
  scabies, *iii*, 2155
  scabs, *iii*, 2074
  scalds, *iii*, 2082
  scarlet fever, *iii*, 2076
  scar tissue, *iii*, 2115
  Schoenlein's achorion, *iii*, 2149
  scleroderma, *iii*, 2170
  scrofuloderma, *iii*, 2101
  scurvy, *iii*, 2073, 2074
  sebocystomatosis, *iii*, 2217
  seborrhea, *iii*, 2216
Skin, skin glands, *iii*, 2216
  skin oxidase, *ii*, 1284
  smallpox, *iii*, 2091, **2093, 2094**
  soft chancre, *iii*, 2113
  spirocheta pallida, *iii*, 2131
  sporotrichosis, *iii*, 2153
  spots, *iii*, 2074
  stigmata, *iii*, 2072
  sweat-glands, *iii*, 2220
  sycosis, *iii*, 2104, 2154
  symmetrical gangrene, *iii*, 2110, 2147
  syphilis, *iii*, 2088, 2098, 2108, **2129, 2130, 2135,** 2165
  syringoma, *iii*, 2199
  tattooing, *i*, 216, 254
  tinea, *iii*, 2152
  toxic edema, *iii*, 2070
  trauma, *iii*, 2072
  tuberculosis, *i*, 258, *iii*, **2122, 2123**
  tumors, *iii*, 2109, 2115, **2121,** 2126, **2127,** 2144, 2160, 2172, **2173,** 2174, 2176, **2177, 2178,** 2179, 2180, **2181, 2185, 2186, 2187, 2189,** 2191, **2193, 2194,** 2196, **2199, 2200**
  ulcer perforating of heel, *iii*, 2109
  ulcers, *iii*, 2074, 2079, 2111, 2113
  ulcers of leg, *iii*, **2112, 2136,** 2158
  uremia, *iii*, 2078
  varicella, *iii*, 2096
  variola, *iii*, 2092
  varioloid, *iii*, 2092
  veruga, *iii*, 2166, 2187
  vesicles, *iii*, 2074
  viteligo, *iii*, 2164
  warts, *iii*, 2187
  Werlhoffs dis., *iii*, 2073
  white spot disease, *iii*, 2165
  xanthelasma, *iii*, 2065
  xanthoma, *iii*, **2160**
  xanthosis, *iii*, 2161
  xeroderma, *iii*, 2163, 2216
  x-ray burns, *iii*, 2083, 2114
Skull, acromegaly, *ii*, 1114
  atrophy, *ii*, **1065**
  birth trauma, *ii*, 1810, 1811
  caries, *ii*, 1139
  contracoup, *ii*, 1190
  cranio-tabes, *ii*, 1165
  deformities, *ii*, 1189
  dysostosis, *ii*, 1190
  exostoses, *ii*, **1199**
  fissures, *ii*, 1084
  fractures, *ii*, 1217, 1943
  hematoma, *ii*, 1093
  hydrocephalus, *ii*, 1165, **1166**
  hyperostosis, *ii*, 1112
  infections, *i*, 159
  kyphosis, *ii*, 1163
  leontiasis, *ii*, **1112**
  macrocephaly, *ii*, 1188
  microcephaly, *ii*, 1189
  myelomas, *ii*, **1218**
  necrosis, *ii*, **1138**
  ostitis deformans, *ii*, 1145
  ostitis-fibrous, *ii*, 1110

Skull, Paget's disease, *ii*, **1108**
  rachitis, *ii*, 1164
  sarcoma, *ii*, **1193**
  sclerosis, *ii*, 1143
  scoliosis, *ii*, 1267
  sella turcica, *iii*, 1950
  synostosis, premature, *ii*, 1184
  syphilis, *ii*, **1138, 1139, 1140, 1141, 1143,** 1144
  tête carré, *ii*, 1165
  trauma, *i*, 296, *iii*, 1943
  tuberculosis, *ii*, 1131
  tumors, *ii*, 1139
Sleeping sickness, *i*, 211, 212
Smallpox, babies, *iii*, **2093, 2094**
  larynx, *i*, 319
  mouth, *i*, 548
  skin, *iii*, 2091
Smegma bacilli, *ii*, 1534
Solar plexus, *ii*, 1024
Spermatic cord, *ii*, 1476
  hydrocele, *ii*, 1484, 1511, **1512**
  tumors, *ii*, 1415, 1537
  varicocele, *ii*, 1401
  vas., *ii*, 1478
Spermatorrhea, *ii*, 1518
Spermatozoa, *ii*, 1510
Spina bifida, *ii*, 1165, *iii*, **1972,** 1975
Spina ventosa, *ii*, 1128
Spinal canal, *iii*, 1830
  lumbar puncture, *iii*, 1830
  spinal fluid, *iii*, 1805, 1846
Spinal column, actinomycosis, *ii*, **1146**
  atrophy, *ii*, 1066, 1069
  carcinoma, *ii*, 1224, *iii*, **2008**
  kyphoscoliosis, *ii*, 1266
  kyphosis, *ii*, 1066
  osteomalacea, *ii*, 1073
  rachischisis, *iii*, 1971
  rachitis, *ii*, 1163
  scoliosis, *ii*, 1066, 1079, 1163
  tuberculosis, *ii*, 1127, 1129, **1132**
Spinal cord, *iii*, 1960
  abscesses, *iii*, 1987
  amyotrophic sclerosis, *iii*, **1995**
  ataxia, *iii*, 2005
  atrophy, *iii*, 1981, 1996
  Brown-Sequard's paraplegia, *iii*, 1985
  caisson disease, *iii*, 2009
  carcinoma, *iii*, 1964, 2012
  cauda equina, *iii*, 1984
  Charcot's dis., *iii*, 1960
  children, *iii*, 1961, 1990
  compression, *ii*, 1130
  concussion, *iii*, 1968
  cysticercus, *iii*, 1964, 1990, 2012
  deformities, *iii*, 1971
  degeneration, *iii*, **1981, 1983**
  dura, *iii*, 1961
  echinococcus, *iii*, 1939
  endothelioma, *iii*, **1963**
  Friedreich's dis., *iii*, 2005
  ganglion, *iii*, **1968**
  glioma, *iii*, 1967, 2011
  hemorrhage, *iii*, 1961
Spinal cord, histological changes, *iii*, 1981
  hydromyelia, *iii*, 1971, 1977
  hydrorachis, *iii*, 1971
  infections, *iii*, 1986, 1988
  inflammation, *iii*, 1961
  Landrey's paralysis, *iii*, 1993
  leprosy, *ii*, 1011
  lumbar puncture, *iii*, 1830
  malformation, *iii*, 1971
  meninges, *iii*, 1959
  meningocele, *iii*, 1975
  Morvan's, *iii*, 1981
  motor neurons, *iii*, 1987
  muscular atrophy, *iii*, 1996
  myasthenic paralysis, *iii*, 1995
  myelitis, *iii*, 1985
  nerves, *iii*, **1960,** 1969, **2012**
  pachymeningitis, *iii*, 1961
  paralysis, progressive bulbar, *iii*, 1995
  paraparesis, *iii*, 1997
  paraplegia, *iii*, 1985
  parasites, *iii*, 1963, 1975, 2012, 2020
  pellagra, *iii*, **2002**
  poisons, *iii*, 1961, 1981, 1987, 1994
  poliomyelitis, ac. ant., *iii*, 1990
  progress. chr. poliomyelitis, *iii*, 1993
  pyramidal tract, *iii*, 1866, 1870
  rachischisis, *iii*, 1971
  sarcoma, *iii*, 1964, 1966, 2012
  sclerosis, *iii*, 1912, 1994, 1995, 1997
  sensory tract, *iii*, 1997
  spina bifida, *iii*, **1972,** 1975
  spinal fluid, *iii*, 1805, 1846
  syphilis, *iii*, 2001, 2011
  syringomyelia, *iii*, 1977, **1978, 1985**
  systemic diseases, *iii*, 2004
  tabes dorsalis, *iii*, 1998
  tracts, *iii*, 1997, **2000**
  trauma, *iii*, 1968, 2005, **2006**
  tuberculosis, *iii*, 2008, 2010
  tumors, *iii*, **1963,** 1980, 2011
Spinal hemorrhage in newborn, *iii*, 1961
Spinal nerves, *iii*, 1960
Spinal paralysis in children, *iii*, 1990
Spirillum, *i*, 211, 411, 613
Spirochetae, *ii*, 1286
  in gall bladder, *ii*, 1020
  icterogenes, *i*, 214, 219
  pallida, *i*, 190, 411, *iii*, 2131
  recurrens, *i*, 782
Spleen, *i*, 216, 217
  abscess, *i*, **233**
  accessory s., *i*, 220
  actinomycosis, *i*, 243
  aleukemia, *i*, 239, 624
  amyloid degeneration, *i*, **244**
  anemia, *i*, 193, 223
  anomalies, *i*, 220
  atrophy, *i*, 224, 243
  Banti's disease, *i*, 219, 224, 225
  carcinoma, *i*, 247
  circulation, *i*, 216, 218, 223
  cyanosis, *i*, 223
  cysts, *i*, 246
  degenerations, *i*, 243

Spleen, diabetes, *i*, 237
  displacement, *i*, 221
  echinococci, *i*, **247**
  embolism, *i*, 226, 227
  enlargement, *i*, 223, 226, 231
  fat absorption, *i*, 220
  focal diseases, *i*, 234
  floating spleen, *i*, 221
  function, *i*, 187, 195
  function, vicarious, *i*, 219
  gas edema, *iii*, **2043**
  Gaucher's type, *i*, 236
  glanders, *i*, 243
  granulomas, infect., *i*, 240
  hemorrhage, *i*, 227, 229
  hyperemia, *i*, 223
  hyperplasia, *i*, 231, 234, 239
  icterus, *i*, 192, 222
  infarct, *i*, **227**, 229
  inflammation, *i*, 230
  iron metabolism, *i*, 219
  kala-azar, *i*, 236
  leprosy, *i*, 243
  leukemia, *i*, 202, 232, 238, 264
  lymphadenoid tissue, *i*, 202
  lymphadenopathy, follicular, *i*, 267
  lymphangioma, *i*, **247**
  lymphatics, *i*, 218
  lymphogranulomatosis, *i*, 239
  malaria, *i*, 222, 235
  Malpighian corpuscles, *i*, 216
  metabolism, *i*, 219
  metastases, *iii*, **1665**
  Mikulicz's disease, 604
  parasites, *i*, 236, 245
  parasplenitis, *i*, 233
  perisplenitis, *i*, 245
  pigment, *i*, 222
  plague, bubonic, *i*, 232
  porphyry spleen, *i*, 339
  pulp, *i*, 217
  rupture, *i*, 232, 235
  sarcoma, *i*, 246
  scars, *i*, 228
  sinusoids, *i*, **230**
  size, *i*, 218
  splenectomy, *i*, 192, 219, 220
  splenic artery, *i*, 216, 218, 220
  splenic tumor, *i*, 223, 226, 232, 234
  splenic vein, *i*, 220
  splenitis, *i*, 233
  splenocytes, *i*, 217
  splenomegaly, *i*, 192, 226, 236
  subphrenic abscess, *i*, 233, 245
  syphilis, *i*, 225, 235, 240
  trauma, *i*, 220, 233
  tropical splenomegaly, *i*, 236
  trypanosoma, *i*, 336
  tuberculosis, *i*, **241**
  tumors, *i*, 202, 223, 226, 232, 235, 245
  typhoid, *i*, 231
  varices, *i*, 230
  veins, *i*, 218
  weight, *i*, 218, 240
  xanthelasmic diseases, *i*, 237

Splenic vein, thrombosis, *i*, 229
Spondilolisthesis, *ii*, 1263, 1268
  spondilitis, *ii*, **1245**
Sporotrichosis, *i*, 621, *ii*, 1147, 1490
Sporozoa, *ii*, 854
Sporozoids, *i*, 209
Spotted fever, *i*, 781
Stains, *i*, 392, 423, 608, 611
Stasis, intestinal, *i*, 754, 777
Status lymphaticus, *i*, 499
Stegomya, *ii*, 1020
Stenosis, aorta, *i*, 91
  bronchi, *i*, 350
  capillaries, *i*, 171
  congenital of aorta, *i*, 28, 47
  esophagus, *i*, 632, 648
  heart, *i*, 40, 42, 45, 91, 93
  intestines, *i*, 747
  Stenson's duct, *i*, 593
  stomach, *i*, 660, 713
Stipple cells in basophilic deg., *i*, 188
Stomach, *i*, 657
  adenoma, *i*, 690
  anatomy, *i*, 657
  anemia, *i*, 661
  anomalies, *i*, 660
  anthrax, *i*, 670
  atrophy, *i*, 667
  autodigestion, *i*, 659
  blood in stomach, *i*, 664
  carcinoma, *i*, 687, 694, **695, 696, 697, 698, 700, 701, 703, 704, 705, 707, 708, 709**
  cardia, *i*, **709**
  catarrh, *i*, 665
  circulation, *i*, 661
  contraction, *i*, 668
  corrosive poisons, *i*, 674
  degenerations, *i*, 712
  dilatation, *i*, 713
  diverticuli, *i*, 716
  erosions, *i*, **662**
  eructation, *i*, 715
  foreign bodies, *i*, 717
  gastritis, *i*, 666, 713
  gastromalacia, *i*, 658
  hemorrhages, *i*, 661, **662**, 664, 686
  hour glass stomach, *i*, 660, 687
  hydrochloric acid, *i*, 657, 679, 708
  infections, *i*, 670, 672
  inflammation, *i*, 665
  lymphogranulomatoris, *i*, 672
  marginal ulcer, *i*, **688**
  melena, *i*, 663
  perforation, *i*, 664, 672, **681, 682, 683,** 685
  pernicious anemia, *i*, 668, 713
  phlegmons, *i*, 669
  poisoning, *i*, 672, 713
  post mortem findings, *i*, 658, 675, 714
  pseudomembrane, *i*, 669
  ptosis, *i*, 716
  pylorospasm, *i*, 660
  pylorus, *i*, 698, **701, 702**
  sarcoma, *i*, 692, **693**
  scars, *i*, 670, 685
  stenosis, *i*, 660, 713

Heavy face type denotes an illustration.

Stomach, syphilis, *i*, 671
  transposition, *i*, 661
  trauma, *i*, 678, 689
  tuberculosis, *i*, 670
  tumors, *i*, 690
  typhoid, *i*, 691
  ulcers, *i*, **677, 680, 681, 682, 683, 684, 686, 688, 689**
  volvulus, *i*, 716, 740
  vomiting, *i*, 711, 761
Stomatitis, *i*, 549
  aphthous, *i*, 549
  catarrhal, *i*, 548
  chronic, *i*, 553
  epidemic, *i*, 550
  leukemic, *i*, 553, 559
  mercurial, *i*, 551
  noma, *i*, 552
  phlegmonous, *i*, 550
  pseudomembranous, *i*, 549
  pustular, *i*, 548
  scurvy, *i*, 550
  ulcerative, *i*, 551
  vesicular, *i*, 548
Streptococci, in blood, *i*, 33
  lymph glands, *i*, 258
  puerperal fever, *iii*, 1750
Struma, adrenal, *ii*, 1289
  thyroid, *i*, **508**, 510
  tongue, *i*, 565
Sublimate poisoning kidney, *ii*, 1302
Sublingual cysts, *i*, 507
  glands, *i*, 575
Subphrenic abscess, *ii*, 830
Suffocation, *i*, 321, 382
Sweat glands, *iii*, 2220
Sycosis, *iii*, 2104, 2154
Symmetrical gangrene, *iii*, 2110, 2147
Synarthroses, *ii*, 1228
Synchelia, *i*, 546
Syncytiolysins, *iii*, 1717
Syncytioma, *iii*, 1717, 1722
Syncytium, *iii*, 1712, 1724
Synostosis, *ii*, 1088
Synotia, *i*, 547
Synovitis, *ii*, 1228, 1234, 1243, 1256
Syphilis, adrenal, *ii*, **1286**
  aneurysm, *i*, 135
  aorta, *i*, 17, 56, 82, **124, 125**, 126, **128**, 131, **136**
  arteries, *i*, 123, 136
  bladder, *ii*, 1432
  blood, *i*, 190, 215
  bone, *ii*, 1102, **1134, 1136, 1138, 1139, 1140, 1141, 1142, 1143**
  brain, *iii*, 1915
  bronchi, *i*, 350
  children, *i*, 131
  congenital, *i*, **464**
  epiglottis, *i*, **318**
  esophagus, *i*, 638
  foot, *iii*, **2136, 2139**, 2140
  gall bladder, *ii*, 1001
  gummas, *i*, **465**, *ii*, **938, 940, 943**
  hair, *iii*, 2165
  hands, *iii*, **2135**
  heart, *i*, **24**
  intestines, *i*, 802, *ii*, 842
  joints, *ii*, 1261
  kidneys, *ii*, 1373, **1374**
  larynx, *i*, 316
  lips, *i*, 557
  liver, *ii*, 937, **938, 940, 941, 942, 943**
  lungs, *i*, 461, 462, **465**
  lymph nodes, *i*, 261
  lymphatics, *i*, 175
  meningitis, *iii*, 1916
  mouth, *i*, 553, 556
  muscles, *iii*, **2047**
  nails, *iii*, 2223
  nose, *i*, 289
  pancreas, *ii*, 1032, 1050
  penis, *ii*, 1536
  pharynx, *i*, 620
  phlebitis, *i*, 160
  placenta, *iii*, 1718
  pleura, *i*, 492
  prepuce, *iii*, **2130**
  skin, *iii*, 2137, **2138, 2139, 2140, 2141, 2143**
  skull, *ii*, 1138, 1140, 1144
  spirocheta pallida, *ii*, **1286**
  spleen, *i*, 216, 225, 235, 240
  stomach, *i*, 671
  tabes, *iii*, **2000**
  teeth, *i*, 584
  testicles, *ii*, **1491, 1492**
  thyroid, *i*, 529
  tongue, *i*, **317**, 556
  trachea, *i*, 333
  tubes, *ii*, 1600
  umbilical cord, *iii*, 1734
  urethra, *ii*, 1454
  uterus, *ii*, 1641
  vagina, *ii*, 1695
  veins, *i*, 159
  vessels, *i*, 82, 126, 131
  vulva, *iii*, 1695, 1703
Syringomyelia, *iii*, 1977, **1978, 1983**

Tabes, *i*, 82, 126, *iii*, 1992, **2000**
Talipes calcan., *ii*, 1270
Tapeworms, *ii*, 847, **849**
Tartar formation, *i*, **580**
Tattooing, *i*, 216, 254
Teeth, *i*, 576
  abscess, *i*, 578
  adamantinoma, *i*, 585, **589, 590**
  antrum of Highmore, *i*, 295, 579, 591
  bacteria, *i*, 579
  carcinoma, *i*, 592
  caries, *i*, 576
  cysts, *i*, 296, 586, 588
  decalcification, *i*, 576
  dental osteoma, *i*, 586
  dental tartar, *i*, **580**
  dentine, *i*, 578, 585
  development, *i*, **581**
  embryology, *i*, 580
  empyema of antrum, *i*, 579
  enamel, *i*, 576, 580

Heavy face type denotes an illustration.

Teeth, enamel plug degeneration, *i*, **591**
  epulis, *i*, **573**, *ii*, 1215
  erosion, *i*, 584
  eruption, *i*, 583
  granuloma, *i*, 586
  Hutchinson teeth, *i*, 584
  inflammation, *i*, 578
  malformation, *i*, 584
  maxillary cysts, *i*, 586
  mechanical lesions, *i*, 577
  milk teeth, *i*, **582**
  odontoma, *i*, 585
  osteoma, *i*, 586
  parulis, *i*, 578
  peridontal cysts, *i*, 588
  pulp granuloma, *i*, **578**
  pulpitis, *i*, 577
  pyorrhea, *i*, 578
  root cysts, *i*, 586
  sarcoma, *i*, 573
  syphilis, *i*, 584
  tartar formation, *i*, **580**
  tuberculosis, *i*, 580
  tumors, *i*, 296, 579, 580
Tendons, *iii*, 2062
  bacteria, *iii*, 2062
  crepitation, *iii*, 2062
  gonorrhea, *iii*, 2062
  gout, *iii*, 2063
  hydrops, *iii*, 2063
  hygroma, *iii*, 2063
  inflammation, *iii*, 2062
  myelomas, *iii*, 2064
  rheumatism, *iii*, 2063
  rice bodies, *iii*, 2063
  sarcoma, *iii*, 2064
  syphilis, *iii*, 2064
  tenosynovitis, *iii*, 2062
  trauma, *iii*, 2064
  tuberculosis, *iii*, 2063, **2066**
  tumors, *iii*, 2064
  xanthoma, *iii*, 2064
Tenias, *ii*, 847, **849**
Teratoids, *ii*, 1504, **1505**
Teratomas, coccygeal gland, *i*, 331
  mediastinum, *i*, 504
  ovaries, *ii*, 1568, 1582
  testicles, *ii*, 1503, **1505**, *iii*, 1746
Testicle, *ii*, 1460
  abscess, *ii*, 1484
  actinomycosis, *ii*, **1495**
  artery-spermatic, *ii*, 1461
  atrophy, *ii*, 1510, 1517
  carcinoma, *ii*, **1498, 1499, 1500, 1501, 1502**
  chorion epithelioma, *ii*, **1507, 1508**
  cryptorchism, *ii*, 1476
  cysts, *ii*, 1494
  dermoids, *ii*, 1503
  descent, *ii*, 1462
  echinococcus, *ii*, 1510
  enchondroma, *ii*, 1203
  epididymitis, *ii*, 1475, 1479, 1484, **1487**
  Florence's reaction for semen, *ii*, 1518
  fungus-diseases, *ii*, 1486
  glanders, *ii*, 1494
Testicle, gonorrhea, *ii*, 1484
  gubernaculum, *ii*, 1460, 1476
  gummas, *ii*, **1491, 1492**
  hematocele, *ii*, 1513
  hemorrhage, *ii*, 1483
  hermaphrotism, *ii*, 1466, **1481, 1483**
  homosexuality, *ii*, 1482
  hydrocele, *ii*, 1484, 1511, **1512**
  hypertrophy, *ii*, 1511
  inflammation, *ii*, 1483
  interstitial cells, *ii*, 1479
  leprosy, *ii*, 1493
  malformation, *ii*, 1475
  orchitis, *ii*, 1483, **1485**
  paradidymis, *ii*, 1461
  parasites, *ii*, 1510
  parotid gland, *i*, 594
  periorchitis, *ii*, 1514
  pseudohermaphrotism, *iii*, **1781**
  rejuvenation, *ii*, 1482
  rhabdomyoma, *ii*, **1495**
  sarcoma, *ii*, 1496
  scrotum, *ii*, 1476, 1533
  semen reaction, *ii*, 1518
  seminal vesicles, *ii*, 1515
  senility, *ii*, 1510, 1522
  Sertoli's cells, *i*, 148
  sex characters secondary, *ii*, 1480
  spermatic artery, *ii*, 1461
  spermatic cord, *ii*, 1511
  spermatogenesis, *ii*, 1480, 1482, 1511
  spermatorrhea, *ii*, 1518
  spermatozoa, *ii*, 1510
  sporotrichosis, *ii*, 1490
  Steinach's experiments, *ii*, 1482
  syphilis, *ii*, **1491, 1492**
  teratoids, *ii*, 1504
  teratomas, *ii*, 1503, **1505**
  tuberculosis, *ii*, 1415, **1487**, 1490
  tumors, *ii*, 1415, 1464, 1476, **1495**, 1588
  tunica vaginalis, *ii*, 1415, 1511
  vas deferens, *ii*, 1478
Tetanus, *i*, 213
Tetany, *i*, 526, **540**
Thomsen's myotonia congenit., *iii*, 2049
Thoracic duct, *i*, 172, 176
    carcinoma, *i*, 183
    tuberculosis, *i*, 175, 482
Thorax, barrel chest, *i*, 367
  hematothorax, *i*, 483
Threadworms, *ii*, 852
Thrombi, *i*, 152
  air, *i*, 207
  aneurysms, *i*, **105**, 116, 119
  aorta, *i*, **102, 153**
  bile-thrombi, *ii*, **1014**
  blood platelets, *i*, 171
  capillaries, *i*, 171
  crural vein, *i*, 153
  heart, *i*, 26, 56, **78, 79, 80**, 81
  intestines, *i*, 785
  kidney, *ii*, 1300, 1305
  location, *i*, 153
  organisation, *i*, 152
  placenta, *iii*, **1728**

Thrombi, recanalisation, *i*, **121**, **154**
  renal vein, *ii*, 1401
  thrombocytes, *i*, 186
  thrombolymphangitis, *i*, 174
  thrombopenia, *i*, 193, 2073
  thrombophlebitis, *i*, 154, **157**
  transfusion, *i*, 152
  tumor thrombi, *i*, 170
  veins, *i*, 152
Thrombophlebitis, *i*, 154
  liver, *ii*, **919**
  milk leg, *i*, 158
Thrush, *i*, 549, 561
  breast, *iii*, 1756
  esophagus, *i*, **561**, 652, 657
  mouth, *i*, 549
  tongue, *i*, 560
  vagina, *iii*, 1698
Thymus, *i*, 495
  abscess (Dubois's), *i*, 502
  accessory, *i*, 497
  aplasia, *i*, 498
  asthma, *i*, 499
  Basedow's disease, *i*, 501
  Bednar's cysts, *i*, 502
  blood, *i*, 189
  chromaflin system, *i*, 500
  cysts, *i*, 503
  death, *i*, 499
  dermoid cysts, *i*, 504
  enlargement, *i*, 200
  Hassel's corpuscles, *i*, 502
  hemorrhagic diathesis, *i*, 502
  hyperplasia, *i*, 498
  hypoplasia, *i*, 500
  leukemia, *i*, 501
  lymphatics, *i*, 200
  mediastinal tumors, *i*, 504
  persistence, *i*, 498
  physiology, *i*, 497
  status lymphaticus, *i*, 499
  suicide, *i*, 501
  syphilis, *i*, 502
  teratomas, *i*, 504
  thymectomy, *i*, 497, 501
  thymus death, *i*, 489, 499
  thyroid, *i*, 501
  tuberculosis, *i*, 503
  tumors, *i*, 503
  weight, *i*, 496
Thyroid, *i*, 504
  abscess, *i*, 509
  absense, *i*, 508
  accessory, *i*, 508
  adenoma, *i*, 512
  amyloid degeneration, *i*, 522
  athyreosis, *i*, 508
  Basedow's disease, *i*, 516, **519**
  Bochdalek's duct, *i*, 507
  cachexia, *i*, 527
  calcification, *i*, 521
  carcinoma, *i*, **530**
  circulation, *i*, 508
  cretinism, *i*, 523
  cysts, *i*, **511**, 520
Thyroid, degenerations, *iii*, 1947
  development, *i*, 506
  dwarfism, *ii*, 1181
  echinococcus, *i*, 537
  endocrine relations, *i*, 528
  enlargement, *i*, 510
  exophthalmus, *i*, 516
  fetal adenoma, *i*, 513
  goiter, *i*, 501, 510, **511**, **518**
  goiter-areas, *i*, 505, 523
  Grave's disease, *i*, 516
  gumma, *i*, 529
  hemorrhagic goiter, *i*, 521
  hyalin degeneration, *i*, 521
  hyperemia, *i*, 509
  hyperplasia, *i*, 515
  hyperthyroidism, *i*, 509
  inflammations, *i*, 508, 510
  influenza, *i*, 312, 341, 389, 403
  iodothyreoglobulin, *i*, 528
  larynx, *i*, 504, 508
  malformation, *i*, 506
  malignant cyst-papilloma, *i*, 534
  metastases, *i*, 531
  mongolianism, *i*, 526
  myxedema, *i*, 529, *ii*, 1181
  ossification, *i*, 521
  papillary cyst-adenoma, *i*, 521
  parasites, *i*, 537
  parathyroids, *i*, 507, 538, **540**
  purpura neonatorum, *i*, 509
  ranula, *i*, 507
  sarcoma, *i*, 534, **535**
  struma, *i*, **508**, 510
  syphilis, *i*, 529
  tetany, *i*, 526
  toxic thyroiditis, *i*, 509
  tumors, *i*, 511, 512, 513, 518, 521, **530**, 534, **535**
Ticks, *i*, 212, 214, *iii*, 1912
Tinea, *iii*, 2152
Toes, Osler's nodes, *i*, 38
  clavus, *iii*, 2166
  corns, *iii*, 2166
  exostoses, *ii*, 1199
  mumification, *iii*, **2108**
  tophi, *ii*, 1253
Tongue, *i*, 548
  actinomycosis, *i*, 559
  bacteria, *i*, 559
  Bartholin's duct, *i*, 575
  black hairy tongue, *i*, 564
  Blandin-Nuhn's glands, *i*, 575
  carcinoma, *i*, 566, **568**, **569**, **570**
  cysts, *i*, 507, 574
  enlargement, *i*, 562
  fungiform papillae, *i*, 563
  furry tongue, *i*, 553
  geographical, *i*, 554
  glanders, *i*, 559
  glands, *i*, 507
  glossitis, *i*, 548, 550
  glossocele, *i*, 566
  hyperkeratosis, *i*, 565
  inflammation, *i*, 562

Throngus, keratosis, *i*, 565
  leukemia, *i*, 559
  leukoplakia, *i*, 565, **569**
  lupus, *i*, 555
  macroglossia, *i*, 177, 562
  oidium albicans, *i*, 560
  papill. degen., *i*, **563**
  phlegmon, *i*, 550
  plicated tongue, *i*, 554
  poisons, *i*, 628
  prolapsus, *i*, 572
  ranula, *i*, 507, 574
  scarlet fever, *i*, 548
  struma, *i*, 565
  sublingual and lingual cysts, *i*, 507, 574
  syphilis, *i*, 317, 556
  thrush, *i*, 560
  tuberculosis, *i*, 564, **568, 569, 570**
  varices, *i*, 563
Tonsil lingual, *i*, 619
Tonsils, *i*, 606
  abscess, *i*, 616
  amygdalitis, *i*, 607
  angina, *i* 615
  carcinoma, *i*, 625
  catarrh, *i*, 617
  diphtheria, *i*, 608
  gumma, *i*, 621
  hypertrophy, *i*, 618
  phlegmous, *i*, 616
  syphilis, *i*, 620
  tonsillitis, *i*, 606, **607,** 615, 616
  tuberculosis, *i*, 620
  tumors, *i*, 625
Tophi, *ii*, 1253
  renal, *ii*, 1376
Torsion, intestines, *i*, 722, 746
  ovarian cyst, *ii*, 1565
  pelvis, *ii*, 1267
Torticollis, *iii*, 2046
Toxemia, *i*, 341
Toxic thyroiditis, *i*, 509
Toxins in blood, *i*, 26, 190, 208
  kidney, *ii*, 1303
Trachea, *i*, 327
  amyloid tumors, *i*, 336
  bifurcation, *i*, 305
  branchiogenetic cysts, *i*, **328, 506, 559**
  carcinoma, *i*, 330, 331, 335
  carotid gland, *i*, 330
  catarrh, *i*, 305
  compression, *i*, 489, 499
  croup, *i*, **332**
  cysts, *i*, 330, **335**
  decubital ulcers, *i*, 334, 337
  dilatation, *i*, 334
  diphtheria, *i*, **332**
  diverticuli, *i*, 329, 335
  ecchondrosis, *i*, 335
  erosions, *i*, 334
  fistulas, *i*, 328
  glanders, *i*, 332
  glands, *i*, 306
  granuloma, *i*, **337**
  grippe, *i*, 332
Trachea, hemorrhage, *i*, 337
  inflammations, *i*, 331
  influenza, *i*, 332
  intubation, *i*, 308, 336
  malformation, *i*, 327
  parasites, *i*, 305
  perforation, *i*, 334
  poisons, *i*, 332
  polypoid granuloma, *i*, **337**
  pseudomembrane, *i*, **332**
  sarcoma, *i*, 336
  scars, *i*, 317
  stenosis, *i*, 334
  syphilis, *i*, **333**
  thymus death, *i*, 489, 499
  tracheitis, *i*, 311
  tracheobronchitis, *i*, 305
  tuberculosis, *i*, **315,** 332
  tumors, *i*, 330, 335, 336
  ulcers, *i*, 333
Traction diverticuli of esophagus, *i*, 652
Transfusion of blood, *i*, 185
Transplantation of adrenal, *ii*, 1281
  ovary, *ii*, 1547
Transposition, *i*, 661
Trematodes, *ii*, 856
Trichina spiralis, *i*, 211, 285, 327, *iii*, 2040, **2056, 2057, 2060**
    intestines, *i*, 211
    laryngeal muscles, *i*, 327
    lymph nodes, *i*, 285
    Miescher's tubules, *iii*, **2060**
Trichocephalus, *ii*, **849,** 855
Trichomonas, *i*, 211, **212,** 236, *ii*, **849**
Tricuspids, *i*, 93
Trigone, *ii*, 1459
Trypanosoma, *i*, 211, 212
  Chaga's disease, *i*, 262
Tsetse fly, *i*, 212
Tuberculoids, *iii*, 2118
Tuberculosis, *i*, 422
  adrenals, *ii*, 1282, **1283, 1284**
  aorta, *i*, 17, 82, 131
  arteries, *i*, 131
  attenuated T. B., *i*, 256
  bladder, *ii*, 1430
  blood, *i*, 6, 44, 72
  bone, *ii*, **1052, 1124, 1126, 1127, 1130, 1132**
  bovine, *i*, **490,** *iii*, 1832
  brain, *iii*, **1905, 1914, 1915**
  bronchi, *i*, 333, 343, 348, 351
  cervix, *iii*, 1640, **1675**
  coxitis, *ii*, 1132
  dura, *iii*, 1832
  esophagus, *i*, 637
  gall bladder, *ii*, 1001
  glands, *i*, 340
  healing, *i*, 340
  heart, *i*, 17, 47, 82
  intestines, *i*, 796, **799, 800**
  joints, *ii*, 1255, **1256, 1260**
  kidney, *ii*, 1308, 1322, 1365, **1366, 1369, 1371**
  larynx, *i*, 315

Heavy face type denotes an illustration.

Tuberculosis, liver, *ii*, **934, 935**
  lungs, *i*, 422, (separate index below)
  lymph nodes, *i*, 255
  lymphatics, *i*, 174
  meninges, *iii*, 1832, **1835, 1836**
  miliary, *i*, **432**
  mouth, *i*, 554
  nose, *i*, 295, 297
  ovaries, *ii*, 1551, 1565
  palate, *i*, **620**
  pancreas, *ii*, 1033
  parotid, *i*, 595
  penis, *iii*, 2127
  peribronchial, *i*, 443
  pericardial, *i*, 416
  peritonitis, *ii*, 861, 870
  pharynx, *i*, 619
  placenta, *iii*, 1732
  pleura, *i*, 489
  Pott's disease, *ii*, 1130
  prostate, *ii*, 1431
  pus (tuberculous), *ii*, 1125
  rectum, *i*, 796
  seminal vesicles, *ii*, 1431
  skin, *i*, 258, *iii*, **2122, 2123,** 2127
  spermatic cord, *ii*, 1415
  spleen, *i*, **241**
  spondylitis, *ii*, 1245
  stomach, *i*, 670
  teeth, *i*, 580
  testicle, *ii*, 1431, **1487,** 1490
  thoracic duct, *i*, 175, 482
  thyroid, *i*, 529
  tongue, *i*, **555**
  trachea, *i*, **315,** 332
  tubes, *ii*, **1598**
  ureters, *ii*, 1371
  urethra, *ii*, 1454
  uterus, *iii*, **1639, 1675**
  vagina, *ii*, 1195
  veins, *i*, 159
  vertebrae, *ii*, 1127
  vulva, *iii*, 1703
Tuberculosis of lungs, *i*, 422, **444, 445**
    aneurysm-rupture, *i*, 449, **450**
    bronchopneumonic foci, *i*, 441, 446
    caseation, *i*, **439,** 441
    caseous pneumonia, *i*, 408, 437
    cavity formation, *i*, 446, **448, 450**
    chronic, *i*, 452
    congenital, *i*, 458
    erosion of pulmon. vein, *i*, 429
    fulminant, *i*, 429
    giant cells, *i*, 423
    healing, *i*, 349
    hemoptisis, *i*, 450
    hemorrhage, *i*, 450
    induration, *i*, 451
    infection, *i*, 428, 436, 456
    infiltration, *i*, 440
    inhalation, *i*, 435
    lymphangitis, *i*, 415, 418, 434
    lymphogenous, *i*, 434, 443
    miliary, *i*, 429, 431, **432**
    mixed infection, *i*, 427, 447
Tuberculosis of lungs, peribronchial, *i*, 443
    perivascular, *i*, 443
    pneumonia, *i*, 425, 437, **438, 441, 442**
    predisposition, *i*, 457
    primary stage, *i*, 454
    softening of foci, *i*, 446
    tubercle bacilli, *i*, 422, 425, 428
    tuberculous cirrhosis, *i*, 452
    tuberculosis in history, *i*, 460
Tularemia, *i*, 262
  Ohara's disease, *i*, 262
Tumors, adamantinoma, *i*, 585, **589, 590**
  adenoids, *i*, 301, 308
  adenoma, *i*, 512, 690, 806, *ii*, 954, 1022, 1387, **1388,** *iii*, **1682, 1772, 1948, 2200**
  adrenals, *ii*, 1287
  amputation neuroma, *iii*, 2021
  amyloid tumors, *i*, **263, 326,** 564
  angioma, *i*, 150, 151, 171, 323, *ii*, 852, 952, 1201, *iii*, 1933
  bladder, *ii*, 1424, 1430, 1432, **1433, 1434, 1435, 1437**
  bone, *i*, 291, *ii*, 1191, 1216
  bone marrow, *i*, 168, 291, *ii*, 1193
  brain, *iii*, **1813, 1814, 1816, 1817, 1818, 1820, 1821, 1822, 1838, 1840,** 1908, 1920, **1921, 1922, 1923, 1924, 1925, 1926, 1927, 1928, 1929, 1930, 1935, 1948, 1953, 1962, 1963, 1966**
  breast, *iii*, **1772, 1773, 1775, 1776, 1777, 1778, 1779, 1781, 1783, 1785, 1786, 1788, 1789, 1791, 1792, 1793, 1794, 1795, 1796, 1797, 1800**
  bronchi, *i*, 385
  carcinoma (see there)
  cartilage, *ii*, 1194
  children, *ii*, 1391, **1575,** 1579, *iii*, 1735
  chloroma, *i*, 272, **273,** 274, *ii*, 1221
  cholesteatoma, *iii*, **1840**
  chondroma, *i*, 167, *ii*, 1201
  chorionepithelioma, *i*, **477,** *ii*, **1507, 1508,** *iii*, 1710, **1740, 1741, 1742, 1743,** 1745, 1746, **1935**
  cylindroma, *i*, 182
  cystoma, *ii*, **1560, 1561, 1562**
  cystpapilloma, *i*, 534
  enamel plug granuloma, *i*, **591**
  enchondroma, *i*, 184, *ii*, 1194, 1198, 1202, 1204
  endothelioma, *i*, 175, 178, **180,** 181, **182,** 493, *ii*, **876,** *iii*, **1817, 1818**
  epiphysis cerebri, *iii*, **1957**
  epithelioma, *iii*, **2156, 2198**
  epulis, *i*, **573,** *ii*, 1215
  esophagus, *i*, 639
  fallopian tubes, *ii*, 1600
  fetus, *iii*, 1735
  fibroendothelioma, *iii*, **1817, 1818**
  fibrolipoma, *ii*, **1390**
  fibroma, *i*, 323, **592,** *ii*, 1200
  fibromyoma, *ii*, 1200, 1390, *iii*, 1647
  fibrosarcoma, *iii*, **1647, 1664, 2190**
  gall bladder, *ii*, 1002
  ganglion-neuroma, *iii*, **2023**
  glands, *i*, 270

Tumors, gliomas, *iii*. 1842, **1921, 1922, 1923, 1924, 1925, 1926, 1927, 1928, 1929, 1930**
  granulomas, *i*, 16, 82, 240, 270, 297, **337, 578,** 586, 595, 619, 637, *ii*, 1122, 1536, *iii*, 1730, 2116, **2118, 2119, 2120**
  gums, *i*, **182, 573**
  heart, *i*, 17, **18,** 83
  hemangioma, *ii*, 1201, 1391, *iii*, **2183**
  hemangiosarcoma, *ii*, **1211, 1212**
  hydradenoma, *iii*, **2200**
  hygroma, *i*, **177,** *iii*, **1814,** 2065, **2066**
  hypernephroma, *i*, 167, *ii*, 1225, **1287,** 1290, **1395, 1396, 1397, 1398, 1399, 1400**
  hypophysis cerebri, *ii*, 1180, *iii*, **1948,** 1950, 1952, 1953
  intestines, *i*, 806
  joints, *ii*, 1262
  keratoma, *iii*, 2172
  kidney, *ii*, 1300, 1387, **1390,** 1419, 1421
  larynx, *i*, 320
  leukosarcomatosis, *i*, 279
  lipoma, *i*, 807, *ii*, 1063, 1201, 1391, *iii*, 1783, **2177, 2178**
  liver, *ii*, 852, **880,** 893, 952, **954, 959, 960, 962, 966, 968**
  lungs, *i*, 378, 391, 469, 470, 473, 475, **478, 479**
  lymph vessel tumors, *i*, 174, 177, 178, **180, 182,** 183
  lymphadenocystoma, *i*, 175
  lymphangio-endothelioma, *i*, 179
  lymphangioma, *i*, 177, **247,** 502, *ii*, 1201, *iii*, **2185, 2186, 2187**
  lymphocystoma, *ii*, 1020
  lymphogranuloma, *i*, 239, 264, 267, **624,** 672, *ii*, 954
  lymphoma, *i*, 263, *ii*, 945
  lymphosarcoma, *i*, 174, 179, 274, *ii*, **1275, 1278, 1324**
  maxilla, *i*, **589, 590, 592,** *ii*, **1210**
  mediastinum, *i*, 280, 504
  melanoma, *iii*, 1843
  melanosarcoma, *i*, 246, *iii*, **2193, 2194**
  meninges, *iii*, 1816, 1837, 1838, 1840, 1844, 1932
  mesentery, *ii*, **879**
  mixed tumors, *i*, 593, 597
  mouth, *i*, 556, 564, 565, 566, 568, 572, 573, **602**
  muscles, *iii*, **2029,** 2055
  myeloid chloroma, *i*, **273**
  myeloma, *i*, 291, *ii*, **1218**
  myoma, *i*, 806, *iii*, 1646
  myxoma, *i*, 301, *ii*, 1220
  myxosarcoma, *ii*, **873,** *iii*, **2191**
  nails, *iii*, 2224
  nerves, *iii*, **1842,** 1936, 1963, 2014, 2021, **2023, 2031**
  neurinoma, *iii*, **2027**
  neuroblastoma, *ii*, 1288
  neuroma, *i*, 492, *iii*, 1931, 2021, 2023
  nose, *i*, 293, 301, 304
  odontoma, *i*, 585
  osteochondroma, *i*, **592,** *ii*, 1206
  osteofibroma, *ii*, **1194**

Tumors, osteoid chondroma, *ii*, 1152
  osteoid sarcoma, *ii*, **1192, 1193,** 1207
  osteoma, *i*, 586, *ii*, 1195, 1196, *iii*, **1821,** 2053, **2054**
  osteosarcoma, *ii*, **1194, 1209, 1210**
  ovary, *ii*, 1555, 1557, **1575, 1576**
  palate, *i*, 622
  pancreas, *ii*, 1022, 1044
  papillary cystadenoma, *i*, 521
  papilloma, *i*, 310, 320, 321, 324, 565, *ii*. **1433, 1434**
  paraffinoma, *iii*, **2121**
  paraganglioma, *ii*, 1287, 1289
  parotid, *i*, 181, 593, 597
  pelvis, *ii*, **1204**
  penis, *ii*, 1538, **1539**
  pericardium, *i*, 17, 83
  periosteum, *ii*, **1209**
  perithelioma, *i*, 178
  peritoneum, *ii*, 861, 872
  pharynx, *i*, 621, 622, 623, **624,** 625, 634
  pia, *iii*, **1838,** 1960
  pineal gland, *iii*, **1957**
  pituitary gland, *ii*, 1180, *iii*, 1948, 1950, 1952, 1953
  placenta, *iii*, 1730, 1733
  plasmacytoma, *i*, 272, 564, 625
  pleura, *i*, 492, 494, 495
  polyps, *i*, 296, 301, **302,** 311, 316, 320, 337, 622, 746, 760, 775, **810, 811, 812,** *ii*, **1433, 1434,** *iii*, **1633, 1654, 1739**
  pregnancy, *iii*, **1722, 1725, 1740, 1741, 1742,** 1743
  prostate, *i*, 175, *ii*, **1529, 1530, 1531, 1532**
  psammofibroma, *iii*, **1817, 1818**
  psammoma, *iii*, **1816**
  psammosarcoma, *iii*, **1820, 1821**
  pseudomyxoma, *ii*, 1565
  pulp granuloma, *i*, 586
  pylorus, *i*, 693
  rectum, *i*, **809, 814,** *ii*, **826**
  retina, *iii*, 1920
  retroperitoneal, *ii*, 873
  rhabdomyoma, *i*, **84,** 572, *ii*, **1394, 1437, 1495, 1532,** *iii*, 1696, 2055
  sacral tumors, *iii*, 1976
  salivary glands, *i*, 181, **598,** 602
  sarcoma, (see there) scalp, *iii*, **2116, 2118, 2119, 2120, 2220**
  scrotum, *ii*, 1537, 1540
  sex organs, *ii*, 1464, **1495,** 1587
  skin, *iii*, 2115, 2160, 2172, **2175, 2178**
  skull, *ii*, 1139, **1193, 1218**
  spinal column, *ii*, 1224, *iii*, 2008
  spinal cord, *iii*, 1911, **1963, 1966,** 1967, 2012
  spleen, *i*, 202, 223, 232, 235, 245
  stomach, *i*, **692, 693, 695, 696, 697, 698, 700, 701, 703, 704, 705, 707, 708, 709**
  syncytioma, *iii*, 1717, 1722
  teeth, *i*, **573, 578,** 586, **589, 590, 591, 592**
  tendons, *iii*, 2064
  teratoma, *i*, 331, 504, *ii*, **1505,** 1568, 1582
  testicles, *ii*, 1476, **1495,** 1496, **1498, 1499, 1500, 1501, 1502,** 1504, **1505, 1507, 1508**

Tumors, thymus, *i*, 503, 504
  thyroid, *i*, 529, **530, 535**
  tongue, *i*, 564, **568, 569, 570,** 572
  trachea, *i*, 330, **331,** 336
  umbilicus, *iii*, 1735
  ureters, *ii*, **1406, 1408**
  urethra, *ii*, 1453, 1454, 1455
  uterus, *iii*, **1633,** 1647 to 1652, 1654 to 1660, 1664, 1665, 1668, 1673 to 1676, 1678, 1680
  vagina, *iii*, 1696, 1697, 1698
  veins, *i*, 151, 158, 167
  vertebrae, *ii*, **1204,** *iii*, **2008**
  vulva, *iii*, 1697, 1703, 1704, **1705,** 1706, **1722, 1723, 1725, 2200**
Tunica vaginalis, *ii*, 1415, 1511
Turbinates, *i*, 293
Typhlitis, *ii*, 831
Typhoid, *i*, 231, **318,** 621, 761, 765, 774, 781, 783, 785, 787, **788, 789, 790, 791, 792,** *ii*, 981, 1001, 1096
Tyson's glands, *ii*, 1533

ULCERS, bladder, *ii*, 1428, 1432
  bronchi, *i*, 333, 337, 352
  duodenal, *iii*, 2082
  epiglottis, *i*, **314**
  esophagus, *i*, 633
  intestines, *i*, 753, 765, 774, 779, *ii*, 829
  joints, *ii*, 1231
  larynx, *i*, 314, 315, 317
  leg, *i*, 169, *ii*, 1106
  marginal, *i*, **688**
  nose, *i*, 297
  stomach, *i*, 677, 680, 684, 689
  typhoid, *i*, **788, 789, 790, 791**
  uterus, *ii*, 1612, *iii*, 1635
  vulva, *iii*, 2086
Umbilicus, *iii*, 1711
  cord, *iii*, 1733
  fistula, *i*, 726
  granuloma, *iii*, 1730
  hernia, *i*, 735
  infection, *iii*, 1732
  syphilis, *iii*, 1734
  tumors, *iii*, 1735
  Wharton's jelly, *iii*, 1733
Urachus, *ii*, 1422
Urate calculi, *ii*, 1412
Uremia, *i*, 15, *ii*, 1300, 1310, 1342
Ureters, *ii*, 1297
  anomalies, *ii*, 1296
  calculi, *ii*, **1409,** 1415
  circulation, *ii*, 1304
  cysts, *ii*, 1297
  hydronephrosis, *ii*, **1406, 1408**
  hydroureters, *ii*, 1297
  kinking, *ii*, 1299
  obstruction, *ii*, 1414
  stenosis, *ii*, 1405
  torsion, *ii*, 1299
  trauma, *ii*, 1405
  ureteritis, *ii*, 1416, **1418**
Urethra, *ii*, 1448, *iii*, 1700
  abscess, *ii*, 1455

Urethra, bacteria, *ii*, 1449, 1453
  bladder, *ii*, 1424, 1448
  calculi, *ii*, **1442**
  carcinoma, *ii*, 1454
  caruncle, *ii*, 1458
  catheters, *ii*, 1455
  chancre, soft, *ii*, 1454
  Cowper's glands, *ii*, 1448, 1453
  cysts, *ii*, 1453
  female meatus, *ii*, 1453, *iii*, 1702
  fistulae, *ii*, 1456
  fracture, *ii*, 1455
  glands, *ii*, 1448
  gonorrhea, *ii*, 1449, 1456
  granuloma, *ii*, 1454
  inflammation, *ii*, 1450
  late gonorrhea, *ii*, 1450
  Littre's glands, *ii*, 1451, 1453
  malformation, *ii*, 1424, 1448
  perforation, *ii*, 1519
  prostate, *ii*, 1448, 1453
  sarcoma, *ii*, 1455
  stricture, *ii*, 1455, 1456
  syphilis, *ii*, 1454
  trauma, *ii*, 1455
  trigone, *ii*, 1459
  tuberculosis, *ii*, 1454
  tumors, *ii*, 1454
  urethral caruncle, *ii*, 1453
Urine, albuminuria, *ii*, 1317, 1325
  anuria, *ii*, 1300, 1340
  bladder, *ii*, 1424
  calculi, *ii*, 1412, **1441, 1442**
  casts, *ii*, 1326, 1327
  chyluria, *i*, 210
  congestion, *ii*, 1301
  cylindruria, *ii*, 1317
  cystitis, *ii*, 1429, 1528
  glycosuria, *iii*, 1951
  hematochyluria, *ii*, 1447
  hematuria, *ii*, 1416, 1528
  juvenile albuminuria, *ii*, 1325
  lipoiduria, *ii*, 1321
  malaria, *i*, 210
  melanuria, *i*, 210, 212
  oliguria, *ii*, 1319, 1340
  parasites, *ii*, 1447
  polyuria, *ii*, 1529
  prostate, *ii*, 1522
  protective colloids, *ii*, 1414
  sediments, *ii*, 1414
  stasis, *ii*, 1415
Urticaria, *iii*, 2079, 2080
Uterus, *ii*, 1464, 1611, *iii*, 1708
  abdominal pressure, *iii*, 1614
  abortion, *ii*, 1621, 1632, *iii*, 1737
  actinomycosis, *iii*, 1641
  adenoma, *iii*, 1661, 1663, 1672, 1682
  adenomyoma, *iii*, 1662
  adenomyometritis, *iii*, **1660**
  adhesions, *ii*, 1611, 1612
  anemia, *iii*, 1634
  anteflexion, *ii*, 1611
  apoplexy, *ii*, 1622
  arbor vitae, *iii*, 1638

Uterus, artery, *i*, **106**
  atresia, *ii*, 1615
  bacteria, *iii*, 1749, 1755
  bicornus, *ii*, **1473**
  birth trauma, *ii*, 1617
  blood mole, *iii*, 1736
  carcinoma, *ii*, 1625, *iii*, 1634, 1640, 1667, **1673, 1674, 1675, 1676, 1678, 1680, 1682, 1684**, 1685, 1687
  cervicitis, *ii*, 1626, 1630, *iii*, 1643, 1669
  cervix, *iii*, 1669, **1678**
  Cesarean section, *ii*, 1617
  childbirth, *ii*, 1614
  chorionepithelioma, *ii*, 1552, *iii*, 1698, 1740, 1741, 1742, 1743
  circulation, *ii*, 1617
  climacterium, *iii*, 1681
  curettage, *iii*, 1689
  cystadenoma, *iii*, 1661
  cystocele, *ii*, 1612
  decidua, *iii*, 1708
  delivery tears, *ii*, 1615
  diverticuli, *ii*, 1617
  dysmenorrhea, *ii*, 1620
  echinococcus, *iii*, 1691
  eclampsia, *iii*, 1717
  ectopic gest., *ii*, 1604
  embryology, *ii*, 1461
  endometritis, *ii*, 1623, *iii*, 1643
  endometrium, *ii*, 1617, 1629
  erosions, *ii*, 1612, *iii*, **1635**
  eversion, *ii*, 1638
  fetal membranes, *iii*, 1710, 1719
  fibrinorrhea, *ii*, 1621
  fibromas, *iii*, **1647, 1648, 1649, 1655, 1656, 1657**
  gonorrhea, *ii*, 1631, *iii*, 1643, 1718
  gynatresia, *ii*, 1616
  heart failure, *ii*, 1623
  hematocele, *ii*, 1623
  hematoma, *ii*, 1623
  hematometra, *ii*, 1616
  hemorrhages, *ii*, 1617, 1622, 1627
  hydatidiform mole, *ii*, 1552, *iii*, 1698
  hydrometra, *ii*, 1616
  hyperplasia, *ii*, 1622, **1626**, 1629
  hypoplasia, *ii*, **1471**, 1472, *ii*, **1473, 1474**
  infections, *ii*, 1748
  inflammations, *ii*, 1623
  inversion, *ii*, 1615
  involution, *iii*, 1718
  ligaments, *ii*, 1612, 1616
  lochia, *iii*, 1717
  malformation, *ii*, **1471, 1473, 1474**
  membranous dysmenorrhea, *ii*, 1620
  menorrhagia, *ii*, 1620
  menstruation, *ii*, 1618, 1619, 1620, 1628
  metaplasia, *iii*, 1689
  metritis, *iii*, 1660
  metrorrhagia, *ii*, 1622
  mole formation, *ii*, 1552, *iii*, 1636, 1698
  myomas, *iii*, 1646, **1647, 1648, 1649, 1650, 1651, 1652, 1658, 1659**
  myometrium, *iii*, 1641
  os uteri, *ii*, 1612, 1626, *iii*, 1641
Uterus, papillary adenocarcinoma, *iii*, **1686**
  parametritis, *iii*, 1645
  passive congestion, *ii*, 1623
  pelvic diaphragm, *ii*, 1614
  perimetritis, *iii*, 1644
  peritonitis, *iii*, 1644
  phlebectasis, *ii*, 1623
  physometra, *ii*, 1616
  placenta, *ii*, 1617, 1622, *iii*, 1700, 1710
  polyps, *ii*, 1625, **1633, 1654**, 1669, 1672
  positions, *ii*, 1611
  post mortem findings, *iii*, 1748
  pregnancy, *ii*, 1618, *iii*, 1708
  prolapsus, *ii*, 1612, **1613**, *iii*, 1634, 1637
  pseudomembranous inflammation, *iii*, 1638
  pseudomyxoma, *ii*, 1565
  puerperal infection, *ii*, 1624, *iii*, 1708, 1717
  puerperium, *ii*, 1624, 1632, *iii*, 1642
  pyometra, *ii*, 1616
  rectocele, *ii*, 1612
  retroflexion, *ii*, 1615
  retroversion, *ii*, 1611
  rotation, *ii*, 1611
  rupture, *ii*, 1606, 1615, 1616
  sarcoma, *ii*, 1620, *iii*, **1664, 1668**, 1670, **1686**
  sarcomatous degeneration, *iii*, **1665**
  secretions, *ii*, 1618
  senility, *ii*, 1615
  stenosis, *ii*, 1615
  syncytium, *ii*, 1552
  syphilis, *iii*, 1641
  trauma, *ii*, 1615
  tuberculosis, *iii*, 1638, **1639**
  tumors, *iii*, **1633, 1647, 1648, 1649, 1650, 1651, 1652, 1654, 1655, 1656, 1657, 1658, 1659, 1660, 1664, 1665, 1668, 1673, 1674, 1675, 1676, 1678, 1680, 1682, 1684, 1685, 1686, 1687**
  tympany, *ii*, 1615
  ulcers, *ii*, 1612, *iii*, 1635
  uremia, *ii*, 1624
  uterine artery, *i*, **106**
Uvula, 605

Vagina, *ii*, 1464, *iii*, 1691
  absorption of poisons, *iii*, 1692
  bacteria, *iii*, 1691
  carcinoma, *iii*, 1697
  catarrh, *iii*, 1692
  childbirth, *iii*, 1699
  children, *iii*, 1693, 1697, 1698
  chorionepithelioma, *iii*, 1698
  colpitis, *iii*, 1692
  colpohyperplasia, *iii*, 1696
  condylomas, *iii*, 1696
  cystocele, *iii*, 1699
  cysts, *iii*, 1695
  diphtheria, *iii*, 1694
  fistulas, *iii*, 1699, 1700, 1708
  foreign bodies, *iii*, 1691, 1700
  gangrene, *iii*, 1694, 1700
  garrulitis, *iii*, 1692
  gas cysts, *iii*, 1696
  glands, *iii*, 1691

Heavy face type denotes an illustration.

- Vagina, gonorrhea, *iii*, 1693
  - gonorrhea in children, *iii*, 1693
  - Haller's stripes, *iii*, 1692
  - hematocolpos, *ii*, 1616
  - hematoma, *iii*, 1699
  - hydatidiform mole, *iii*, 1698
  - hymen, *ii*, 1616, *iii*, 1691
  - inversion, *ii*, 1614
  - mercury poisoning, *iii*, 1692, 1694
  - metastases, *iii*, 1669, 1698
  - oxyuris, *iii*, 1698
  - parasites, *iii*, 1698
  - phlegmon, *iii*, 1694
  - poisons, *iii*, 1699
  - position changes, *iii*, 1699
  - proctitis, *iii*, 1693
  - prolapsus, *ii*, 1612, **1613**, *iii*, 1699
  - pseudomembrane, *iii*, 1693
  - puerperal fever, *iii*, 1691
  - rectocele, *iii*, 1699
  - rhabdomyoma, *iii*, 1696
  - sarcoma, *iii*, 1697
  - secretion, *iii*, 1691
  - syphilis, *iii*, 1695
  - thrush, *iii*, 1694
  - trauma, *iii*, 1699
  - tuberculosis, *iii*, 1695
  - tumors, *iii*, 1669, 1696, 1697, 1698
  - ulcers, *iii*, 1692, 1694, 1695
  - vaginitis, *iii*, 1692, 1693
  - varices, *iii*, 1699
  - vulva, *iii*, 1700
  - vulvovaginitis, *iii*, 1701
- Valves, aortic, *i*, 42, 93
  - mitral, *i*, 43
  - pulmonary, *i*, 46
  - tricuspid, *i*, 42, 93
  - valve leaflet vessels, *i*, 22
  - vegetations, *i*, 28, 29, 35
- Vaquez-Osler-erythremia, *i*, 189
- Varicella, *iii*, 2096
- Varices, *i*, 148, 163
  - aneurysmal, *i*, 148
  - esophagus, *i*, 633
  - hydrostatic pressure, *i*, 164
  - of leg, *i*, **163, 169**
  - nerves, *i*, 162
  - pulmonary, *i*, 162
  - rupture, *i*, 162
  - saccular, *i*, 164
  - spleen, *i*, 230
  - testicle, *ii*, 1401
  - tongue, *i*, 563
- Varicocele, *ii*, 1401
- Variola, *i*, 319, 548, *iii*, 2091, 2092, 2093, 2094
  - larynx, *i*, 319
  - vaccine, *iii*, 2096
- Varioloid, *iii*, 2095
- Vas deferens, *ii*, 1478
- Vasa vasorum, *i*, 99, 100, 112, 127, 172
- Vater-Pacini bodies, *ii*, 1050
- Vegetable parasites, *i*, 213
  - of skin, *iii*, **2116, 2118, 2119, 2120, 2149, 2152**
- Veins, *i*, 152
  - actinomycosis, *i*, 160
  - anastomoses, *i*, 166
  - aorta, *i*, **153**
  - bone marrow, *i*, 159
  - caput medusae, *i*, 165
  - carcinoma, *i*, 167
  - cavernous metamorphosis, *i*, **154**
  - chondroma, *i*, 168
  - concretions, *i*, 155
  - crural ulcers, *i*, **169**
  - dilatation, *i*, 160
  - diploe, *i*, 158
  - eclampsia, *i*, 162
  - elephantiasis, *i*, 167
  - embolism, *i*, 155
  - esophagus, *i*, 632
  - hemorrhoids, *i*, 158, 165, **166**
  - hepatic, *ii*, 893
  - hydrostatic pressure, *i*, 163
  - infection, *i*, 156
  - intestines, *i*, 749
  - leg, *i*, 163, 169
  - lymphatics, *i*, 157
  - parasites, *i*, 170
  - phlebectasias, *i*, 160, 162, 166
  - phlebitis, *i*, 156
  - phlebomalacia, *i*, 161
  - phlebosclerosis, *i*, **157**
  - phlegmasia alba dolens, *i*, 158
  - recanalization, *i*, 154
  - renal, *i*, 100, *ii*, 1401
  - retrograde thrombi, *i*, 170, *ii*, 1400
  - rupture, *i*, 162, 167
  - spleen, *i*, 229
  - syphilis, *i*, 159, 167
  - thrombi, *i*, **153**
  - thrombophlebitis, *i*, 150, **157**
  - trauma, *i*, 167
  - tuberculosis, *i*, 159
  - tumor thrombi, *i*, 170, *ii*, 1400, 1401
  - tumors, *i*, 151, 167, 168, 172
  - varicosities, *i*, 162, 163
  - vena cava and hypernephroma, *ii*, 1400
- Ventricles, *i*, 21, *iii*, 1846
  - cerebrospinal fluid, *iii*, 1805, 1846
  - diseases, *iii*, 1846
  - ependyma, *iii*, 1846, 1851
  - heart, *i*, 21
  - hemorrhages, *iii*, 1851
  - hydrocephalus, *iii*, **1847**, 1848, 1849
  - lateral v., *iii*, **1928**
  - parasites, *iii*, 1852
  - puncture, *iii*, 1847
- Verruga, *iii*, **2167**
- Vertebrae, *ii*, **1069**, 1071, 1127, 1131, *iii*, 2008
  - abscesses, *ii*, 1131
  - arthritis deformans, *ii*, 1245
  - carcinoma, *iii*, **2008**
  - enchondroma, *ii*, **1204**
  - fracture, *iii*, **2006**
  - kyphosis, *ii*, 1066, 1120, **1132**, 1264
  - lordosis, *ii*, 1079, 1264
  - Pott's disease, *ii*, **1129**, 1130

Heavy face type denotes an illustration.

Vertebrae, scoliosis, *ii*, 1066, 1163, 1268
  spondylolisthesis, *ii*, 1268
  tuberculosis, *ii*, 1127, 1130, **1132**, *iii*, 2008
Vesicle, seminal, *ii*, 1415, 1431, 1515, 1516, 1517
    calculi, *ii*, 1516
    tumors, *ii*, 1415
Vincent's angina, trench-mouth, *i*, 550, 560, 613, 616
Viscera, *i*, **140**
  transposition, *i*, 661
Viteligo, *iii*, **2164**
Vocal cords, *i*, 305, 310
  false vocal cords, polyps, *i*, **320**
  fibro epithelioma, *i*, **322**
  fibroma, *i*, **322**
Volkmann's perforating canals, *ii*, 1053
Volvulus, *i*, 716, 746
Vomiting, *i*, 711, 761
Vulva, *iii*, 1700
  actinomycosis, *iii*, 1703
  bacteria, *iii*, 1703
  Bartholin's gland, *iii*, 1702, 1707
  castration, *iii*, 1702
  catarrh, *iii*, 1701
  chancre, *iii*, 1703
  circulation, *iii*, 1701
  clitoris, *iii*, 1701, 1705
  condylomas, *iii*, 1704
  cysts, *iii*, 1707
  delivery, *iii*, 1701
  diphtheria, *iii*, 1702
  edema, *iii*, 1701
  elephantiasis, *iii*, **1703**
  fibroma peduncul., *iii*, **1705**
  fistulae, *iii*, 1708
  gangrene, *iii*, 1703
  gonorrhea, *iii*, 1702, 1707
  hematoma, *iii*, 1701
  hemorrhage, *iii*, 1701
  Hottentot apron, *iii*, 1704
  hydatidiform mole, *iii*, **1722, 1723, 1725**
  hydradenoma, *iii*, **2200**
  hymen, *iii*, 1700
  inflammation, *iii*, 1701
  kraurosis, *iii*, 1702
  labia, *iii*, 1700
  labial herpes, *iii*, 2086
Vulva, eukoplakia, *iii*, 1702
  lymphatics, *i*, 176
  masturbation, *iii*, 1704
  mons veneris, *iii*, 1700
  necrosis, *iii*, 1702
  nymphae, *iii*, 1700
  phlegmon, *iii*, 1703
  plasmacytoma, *iii*, 1753
  pruritus, *iii*, 1702
  puerperal ulcers, *iii*, 1701, 1703
  smegma, *iii*, 1706
  syphilis, *iii*, 1695, 1703
  thrombosis, *iii*, 1701
  trauma, *iii*, 1701
  tuberculosis, *iii*, 1703
  tumors, *iii*, 1703, 1705, 1722, 1723, 1725, 1753, 2200
  ulcers, *iii*, 1701, 1703, 1705, 2079
  urethra, *iii*, 1700
  uterine prolapse, *ii*, 1612
  vestibule, *iii*, 1700
  vulvitis, *iii*, 1701
  vulvo vaginitis in children, *iii*, 1701

War gas, *i*, 376
Warts, *iii*, **2167**
Waxy casts, *ii*, 1327
Waxy degeneration of muscles, *iii*, **2037**
Weil's infect. icterus, *i*, 214, 219, *ii*, 1019
Werlhoff's purpura hemorrhagica, *iii*, 2073
Wharton's jelly, *iii*, 1734
Widal reaction, *i*, 785
Wilson's progress. degen. lentic. nucleus, *ii*, 954, **970**, *iii*, 1863
Winkel's fatty card. degen. in new born, *i*, 53
Wolffian duct, *ii*, 1392, **1459**
Wry neck (torticollis), *iii*, 2046

Xanthelasma, *i*, 237, *iii*, 2065
Xanthoma cells, *iii*, 2064
Xanthosis, *iii*, 2161
Xeroderma, *iii*, 2163, 2216

Yellow fever, *i*, 214

Zenker's diverticuli, *i*, 629
Zuckerkandl organs, *ii*, 1277

Heavy face type denotes an illustration.

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